# CONTENTS

## General, physical, and inorganic


| NO. | | PAGE |
|---|---|---|
| 190 | Heats of adsorption of oxygen on solid solutions of uranium dioxide in thorium dioxide at −183°<br>By J. D. M. McConnell | 947 |
| 192 | The infrared spectrum of thioformamide<br>By Mansel Davies and W. Jeremy Jones | 955 |
| 202 | Parachors and molecular structure of some metal alkoxides<br>By D. C. Bradley, (Miss) C. C. A. Prevedorou, J. D. Swanwick, and W. Wardlaw | 1010 |
| 221 | Aluminium phosphates. Part II. Ion-exchange and pH-titration studies of aluminium phosphate complexes in solution<br>By J. E. Salmon and J. G. L. Wall | 1128 |
| 226 | The absorption spectra of some ferrous and ferric complexes<br>By J. C. Tomkinson and R. J. P. Williams | 1153 |
| 232 | A hydrate of potassium dichloroiodide<br>By G. F. Allison and G. H. Cheesman | 1177 |
| 250 | Differential capacity measurements in aqueous and methanolic ammonium chloride, ammonium fluoride, and hydrochloric acid in relation to anion adsorption<br>By A. A. Moussa, H. M. Sammour, and H. A. Ghaly | 1269 |
| Note | | |
| 259 | The electrolytic determination of indium<br>By (the late) H. Terrey and J. Thabit | 1303 |


## Physical organic


| | | |
|---|---|---|
| 186 | The light absorption of pyrroles. Part I. Ultraviolet spectra<br>By Ulli Eisner and P. H. Gore | 922 |
| 187 | Infrared spectra and crystallinity. Part V. Dimethyl and diethyl esters of αω-dicarboxylic acids<br>By P. J. Corish and W. H. T. Davison | 927 |
| 193 | Heats of combustion and molecular structure. Part IV. Aliphatic nitroalkanes and nitric esters<br>By R. C. Cass, S. E. Fletcher, C. T. Mortimer, P. G. Quincey, and H. D. Springall | 958 |
| 195 | The light absorption of pyrroles. Part II. Infrared spectra<br>By Ulli Eisner and R. L. Erskine | 971 |
| 196 | The infrared spectra of *N*-heteroaromatic systems. Part I. The porphins<br>By S. F. Mason | 976 |
| 204 | Heats of combustion. Part II. The six lutidines<br>By J. D. Cox and H. A. Gundry | 1019 |
| 205 | Structure and properties of mesomeric systems. Part I. Resonance energies<br>By David Peters | 1023 |
| 206 | Structure and properties of mesomeric systems. Part II. The chemical reactivity of alternant and non-alternant hydrocarbons<br>By David Peters | 1028 |
| 207 | Structure and properties of mesomeric systems. Part III. Charge distribution and related properties in non-alternant hydrocarbons<br>By David Peters | 1039 |
| 208 | $NH_2$-Stretching frequencies in primary amines<br>By W. J. Orville-Thomas, A. E. Parsons, and C. P. Ogden | 1047 |
| 216 | Conductometric investigation of the rate of hydrolysis of nitriles in 100% sulphuric acid<br>By (Miss) M. Liler and Dj. Kosanovic | 1084 |

| NO. | | PAGE |
|---|---|---|
| 225 | Polymerizations of ethylene in the presence of titanium tetrachloride and certain metal alkyls<br>By J. C. McGowan and B. M. Ford | 1149 |
| 240 | Vibrational frequency correlations in heterocyclic molecules. Part IV. Indoxyl derivatives<br>By S. J. Holt, A. E. Kellie, D. G. O'Sullivan, and P. W. Sadler | 1217 |
| 241 | Researches on monolayers. Part VII. Reactions of casein with dyes and other aromatic solutes and their relation to adsorption by protein fibres<br>By A. Cameron, C. H. Giles, and T. H. MacEwan | 1224 |
| 246 | *N*-Oxides and related compounds. Part VIII. The electric dipole moments of a series of 4-substituted pyridine–boron trichloride complexes<br>By C. M. Bax, A. R. Katritzky, and L. E. Sutton | 1254 |
| 247 | *N*-Oxides and related compounds. Part IX. The electric dipole moments of pyridine– and trimethylamine–boron trihydride and trihalide complexes<br>By C. M. Bax, A. R. Katritzky, and L. E. Sutton | 1258 |
| 248 | *N*-Oxides and related compounds. Part X. The hydrogenation of some pyridine 1-oxides<br>By A. R. Katritzky and A. M. Monro | 1263 |
| 249 | The electric dipole moments of 1 : 2-5 : 6-dibenz*ocyclo*octadiene and *o*-xylene<br>By E. W. Randall and L. E. Sutton | 1266 |
| Notes | | |
| 257 | The effect of urea on the streaming birefringence and viscosity of sodium deoxyribonucleate<br>By A. R. Mathieson and M. R. Porter | 1298 |
| 258 | Fractional precipitation of nucleic acids by ethanol<br>By A. R. Mathieson and M. R. Porter | 1301 |
| 260 | Hydroxyl stretching frequencies of some analogues of 8-hydroxyquinoline<br>By F. J. C. Rossotti and Hazel S. Rossotti | 1304 |


## Organic


| | | |
|---|---|---|
| 185 | The thermal decomposition of 3 : 5-dibromobenzene-1 : 4-diazo-oxide<br>By M. J. S. Dewar and A. N. James | 917 |
| 188 | The application of infrared spectroscopy to a study of some reaction intermediates and products of the autoxidation of long-chain olefins<br>By (Mrs.) J. Gold | 934 |
| 189 | 2 : 3-Benzorubicene, rubicene, and their derivatives<br>By E. Clar and W. Willicks | 942 |
| 191 | Researches on acetylenic compounds. Part LIX. The synthesis of three polyacetylenic antibiotics<br>By P. J. Ashworth, E. R. H. Jones, G. H. Mansfield, K. Schlögl, J. M. Thompson, and M. C. Whiting | 950 |
| 194 | Sesquiterpenoids. Part X. The constitution of lactucin<br>By D. H. R. Barton and C. R. Narayanan | 963 |
| 197 | Synthesis of (±)-crebanine<br>By T. R. Govindachari, K. Nagarajan, and C. V. Ramadas | 983 |
| 198 | 1-Phenylnaphthalenes. Part IV. The cyclisation of methyl hydrogen *cis*- and *trans*-γ-*o*-methoxyphenyl- and ethyl hydrogen *cis*- and *trans*-γ-*p*-methoxyphenyl-γ-phenylitaconate to the corresponding 1-phenylnaphthalenes<br>By F. G. Baddar, Lanson S. El-Assal, and (Mrs.) Victorine B. Baghos | 986 |
| 199 | The behaviour of derivatives of 3 : 4-anhydrogalactose towards acidic reagents. Part I<br>By J. G. Buchanan | 995 |
| 200 | The separation and characterisation of the 2′ : 5′- and 3′ : 5′-diphosphate and the 2′ : 3′ : 5′-triphosphate of adenosine<br>By J. Baddiley, J. G. Buchanan, and R. Letters | 1000 |
| 201 | An anomalous Barbier–Wieland degradation<br>By Wilson Baker, R. F. Curtis, J. F. W. McOmie, L. W. Olive, and V. Rogers | 1007 |


XUM

NO. PAGE

203 Properties of ion pairs formed by proton transfer to methoxyphenylpolyenealdehydes
By A. WASSERMANN . . . . . 1014

209 Formation of free radicals during the preparation of organomagnesium compounds in a hydrocarbon solvent
By D. BRYCE-SMITH and G. F. COX . . . . . 1050

210 Researches on acetylenic compounds. Part LX. The synthesis of three natural polyacetylenic hydrocarbons
By E. R. H. JONES, L. SKATTEBOL, and M. C. WHITING . . . . . 1054

211 The hemicelluloses of European larch (*Larix decidua*). Part I. The constitution of a xylan
By G. O. ASPINALL and J. E. MCKAY . . . . . 1059

212 Alicyclic glycols. Part XIV. The tetralin-2 : 3-diols and the *cyclo*hex-4-ene-1 : 2-diols
By MD. ERFAN ALI and L. N. OWEN . . . . . 1066

213 Alicyclic glycols. Part XV. Some lactols and lactones derived from the *cyclo*hex-4-ene-1 : 2-diols
By MD. ERFAN ALI and L. N. OWEN . . . . . 1074

214 Triphenylene: an examination of modified Mannich syntheses, and an improvement of the Rapson synthesis
By C. C. BARKER, R. G. EMMERSON, and J. D. PERIAM . . . . . 1077

215 5-Methyl-3 : 4-benzofluorene
By B. R. T. KEENE and K. SCHOFIELD . . . . . 1080

217 Identification of two chromogens in the Elson–Morgan determination of hexosamines. A new synthesis of 3-methylpyrrole. Structure of the "pyrrolenephthalides"
By J. W. CORNFORTH and (MRS.) M. E. FIRTH . . . . . 1091

218 The azulene series. Part II. The synthesis and properties of alkoxyazulenes
By D. H. REID, W. H. STAFFORD, and J. P. WARD . . . . . 1100

219 The azulene series. Part III. The synthesis and properties of 3-benzylideneguaiazulenium chloride
By D. H. REID, W. H. STAFFORD, WINIFRED L. STAFFORD, and (in part) G. MCLENNAN and A. VOIGT . . . . . 1110

220 The azulene series. Part IV. The synthesis and properties of 3-acylguaiazulenes
By D. H. REID, W. H. STAFFORD, and WINIFRED L. STAFFORD . . . . 1118

222 Potential tumour-inhibitors based on diazomethane
By J. A. HENDRY, F. L. ROSE, and A. L. WALPOLE . . . . . 1134

223 Acyl *iso*thiocyanates. Part II. Reactions of aroyl *iso*thiocyanates with amines and amino-acids in aqueous solution
By D. T. ELMORE and J. R. OGLE . . . . . 1141

224 5-Alkylacridines. Part I. Synthesis of 5-methylacridine and certain substituted analogues
By A. CAMPBELL, C. S. FRANKLIN, E. N. MORGAN, and D. J. TIVEY . . . 1145

227. Anils. Part I. Syntheses of 9-phenylphenanthridine
By C. A. BARTRAM, D. HARRISON, and (the late) W. F. SHORT . . . . 1158

228 The reaction of chlorine with tetrahydro-2-methylenefuran
By M. F. ANSELL and D. A. THOMAS . . . . . 1163

229 Reduced cyclic compounds. Part III. The preparation and cyclodehydration of some unsaturated tertiary alcohols
By M. F. ANSELL and (the late) M. E. SELLECK . . . . . 1167

230 Fission of di-(3-methyl-1 : 5-diphenyl-4-pyrazolyl) disulphide by chlorine
By W. J. BARRY . . . . . 1171

231 Self-condensation of acetamidoacetaldehyde and of aminoacetone
By J. W. CORNFORTH . . . . . 1174

233 Polynuclear heterocyclic systems. Part XIII. The reaction of ethyl diazoacetate with naphthalene and its heterocyclic analogues
By G. M. BADGER, B. J. CHRISTIE, H. J. RODDA, and JENNETH M. PRYKE . 1179

XUM

| NO. | | PAGE |
|---|---|---|
| 234 | The stereochemistry of triarylstibines. Part II. Synthesis of unsymmetrically substituted triarylstibines and optical resolution of *p*-carboxyphenyl-1-naphthylphenylstibine<br>By I. G. M. CAMPBELL and A. W. WHITE | 1184 |
| 235 | 7-Hydroxychroman and its 6-acetyl compound<br>By P. NAYLOR, G. R. RAMAGE, and F. SCHOFIELD | 1190 |
| 236 | The steric course of alkylation of enols from some *cyclo*hexanones and of hydrogenation of selin-4-ene-3-ones in neutral and alkaline solution<br>By R. HOWE and F. J. MCQUILLIN | 1194 |
| 237 | The alkaline degradation of polysaccharides. Part III. Action of sodium hydroxide on amylose<br>By G. MACHELL and G. N. RICHARDS | 1199 |
| 238 | The alkaline degradation of polysaccharides. Part IV. Monosaccharide analogues of periodate oxycellulose<br>By D. O'MEARA and G. N. RICHARDS | 1204 |
| 239 | The oxidation of monosaccharides by periodate with reference to the formation of intermediary esters<br>By L. HOUGH, T. J. TAYLOR, G. H. S. THOMAS, and B. M. WOODS | 1212 |
| 242 | Chalcones and related compounds. Part IV. Addition of hydrogen cyanide to chalcones<br>By W. DAVEY and D. J. TIVEY | 1230 |
| 243 | Gibberellic acid. Part V. The relation between gibberellin $A_1$ and gibberellic acid<br>By JOHN FREDERICK GROVE, P. W. JEFFS, and T. P. C. MULHOLLAND | 1236 |
| 244 | Synthesis of some angularly bridged cyclic systems. Part I. Perhydrobenz[*d*]-indole<br>By R. D. HAWORTH and A. F. TURNER | 1240 |
| 245 | The synthesis of some substituted hexahydro-12-methyl-2-oxophenanthrenes<br>By F. H. HOWELL and D. A. H. TAYLOR | 1248 |
| 251 | Studies of trifluoroacetic acid. Part XIV. Reaction of acyl trifluoroacetates with 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol<br>By E. J. BOURNE, J. BURDON, and J. C. TATLOW | 1274 |
| 252 | 1 : 2 : 3 : 4 : 5 : 6- and 1 : 2 : 3 : 4 : 5 : 7-Hexamethylnaphthalene<br>By W. CARRUTHERS and J. D. GRAY | 1280 |
| 253 | Phenylation with diazoaminobenzenes<br>By R. L. HARDIE and R. H. THOMSON | 1286 |
| 254 | Decomposition reactions of heterocyclic diacyl peroxides. Part III. 5-Methyl-1-phenyl-1 : 2 : 3-triazole-4-carbonyl peroxide<br>By (the late) M. C. FORD and DONALD MACKAY | 1290 |
| 255 | Decomposition reactions of heterocyclic diacyl peroxides. Part IV. Nicotinoyl peroxide<br>By (the late) M. C. FORD and DONALD MACKAY | 1294 |

NOTES

| | | |
|---|---|---|
| 256 | Some unsymmetrical azo-nitriles<br>By (the late) M. C. FORD and R. A. RUST | 1297 |
| 261 | A common precursor of conhydrine and *pseudo*conhydrine<br>By T. R. GOVINDACHARI and S. RAJAPPA | 1306 |
| 262 | Ring expansion. Part III. The isomerisation of dibenzylidene derivatives of *cyclo*hexanones<br>By R. H. BURNELL | 1307 |
| 263 | A short synthesis of 3-methylfuran<br>By J. W. CORNFORTH | 1310 |
| 264 | Preparation of ketones by cleavage of 2 : 4-dinitrophenylhydrazones<br>By N. M. CULLINANE and B. F. R. EDWARDS | 1311 |
| 265 | 8-Amino*iso*quinoline: a correction<br>By K. SCHOFIELD | 1312 |

# INDEX OF AUTHORS' NAMES


Ali, Md. E., and Owen, L. N., 1066, 1074
Allison, G. F., and Cheesman, G. H., 1177
Ansell, M. F., and Selleck, M. E., 1167
Ansell, M. F., and Thomas, D. A., 1163
Ashworth, P. J., Jones, E. R. H., Mansfield, G. H., Schlögl, K., Thompson, J. M., and Whiting, M. C., 950
Aspinall, G. O., and McKay, J. E., 1059
Baddar, F. G., El-Assal, L. S., and Baghos, V. B., 986
Baddiley, J., Buchanan, J. G., and Letters, R., 1000
Badger, G. M., Christie, B. J., Rodda, H. J., and Pryke, J. M., 1179
Baghos, V. B. See Baddar, F. G., 986
Baker, W., Curtis, R. F., McOmie, J. F. W., Olive, L. W., and Rogers, V., 1007
Barker, C. C., Emmerson, R. G., and Periam, J. D., 1077
Barry, W. J., 1171
Barton, D. H. R., and Narayanan, C. R., 963
Bartram, C. A., Harrison, D., and Short, W. F., 1158
Bax, C. M., Katritzky, A. R., and Sutton, L. E., 1254, 1258
Bourne, E. J., Burdon, J., and Tatlow, J. C., 1274
Bradley, D. C., Prevedorou, C. C. A., Swanwick, J. D., and Wardlaw, W., 1010
Bryce-Smith, D., and Cox, G. F., 1050
Buchanan, J. G., 995
Buchanan, J. G. See also Baddiley, J., 1000
Burdon, J. See Bourne, E. J., 1274
Burnell, R. H., 1307
Cameron, A., Giles, C. H., and MacEwan, T. H., 1224
Campbell, A., Franklin, C. S., Morgan, E. N., and Tivey, D. J., 1145
Campbell, I. G. M., and White, A. W., 1184
Carruthers, W., and Gray, J. D., 1280
Cass, R. C., Fletcher, S. E., Mortimer, C. T., Quincey, P. G., and Springall, H. D., 958
Cheesman, G. H. See Allison, G. F., 1177
Christie, B. J. See Badger, G. M., 1179
Clar, E., and Willicks, W., 942
Corish, P. J., and Davison, W. H. T., 927
Cornforth, J. W., 1174, 1310
Cornforth, J. W., and Firth, M. E., 1091
Cox, G. F. See Bryce-Smith, D., 1050
Cox, J. D., and Gundry, H. A., 1019
Cullinane, N. M., and Edwards, B. F. R., 1311
Curtis, R. F. See Baker, W., 1007
Davey, W., and Tivey, D. J., 1230
Davies, M., and Jones, W. J., 955
Davison, W. H. T. See Corish, P. J., 927
Dewar, M. J. S., and James, A. N., 917
Edwards, B. F. R. See Cullinane, N. M., 1311
Eisner, U., and Erskine, R. L., 971
Eisner, U., and Gore, P. H., 922
El-Assal, L. S. See Baddar, F. G., 986
Elmore, D. T., and Ogle, J. R., 1141
Emmerson, R. G. See Barker, C. C., 1077
Erskine, R. L. See Eisner, U., 971
Firth, M. E. See Cornforth, J. W., 1091
Fletcher, S. E. See Cass, R. C., 958
Ford, B. M. See McGowan, J. C., 1149
Ford, M. C., and Mackay, D., 1290, 1294
Ford, M. C., and Rust, R. A., 1297
Franklin, C. S. See Campbell, A., 1145
Ghaly, H. A. See Moussa, A. A., 1269
Giles, C. H. See Cameron, A., 1224
Gold, J., 934
Gore, P. H. See Eisner, U., 922
Govindachari, T. R., Nagarajan, K., and Ramadas, C. V., 983
Govindachari, T. R., and Rajappa, S., 1306
Gray, J. D. See Carruthers, W., 1280
Grove, John Frederick, Jeffs, P. W., and Mulholland, T. P. C., 1236
Gundry, H. A. See Cox, J. D., 1019
Hardie, R. L., and Thomson, R. H., 1286
Harrison, D. See Bartram, C. A., 1158
Haworth, R. D., and Turner, A. F., 1240
Hendry, J. A., Rose, F. L., and Walpole, A. L., 1134
Holt, S. J., Kellie, A. E., O'Sullivan, D. G., and Sadler, P. W., 1217
Hough, L., Taylor, T. J., Thomas, G. H. S., and Woods, B. M., 1212
Howe, R., and McQuillin, F. J., 1194
Howell, F. H., and Taylor, D. A. H., 1248
James, A. N. See Dewar, M. J. S., 917
Jeffs, P. W. See Grove, John Frederick, 1236
Jones, E. R. H., Skattebøl, L., and Whiting, M. C., 1054
Jones, E. R. H. See also Ashworth, P. J., 950
Jones, W. J. See Davies, M., 955
Katritzky, A. R., and Monro, A. M., 1263
Katritzky, A. R. See also Bax, C. M., 1254, 1258
Keene, B. R. T., and Schofield, K., 1080
Kellie, A. E. See Holt, S. J., 1217
Kosanović, Dj. See Liler, M., 1084
Letters, R. See Baddiley, J., 1000
Liler, M., and Kosanović, Dj., 1084
McConnell, J. D. M., 947
MacEwan, T. H. See Cameron, A., 1224
McGowan, J. C., and Ford, B. M., 1149
Machell, G., and Richards, G. N., 1199
Mackay, D. See Ford, M. C., 1290, 1294
McKay, J. E. See Aspinall, G. O., 1059
McLennan, G. See Reid, D. H., 1110
McOmie, J. F. W. See Baker, W., 1007
McQuillin, F. J. See Howe, R., 1194
Mansfield, G. H. See Ashworth, P. J., 950
Mason, S. F., 976
Mathieson, A. R., and Porter, M. R., 1298, 1301
Monro, A. M. See Katritzky, A. R., 1263
Morgan, E. N. See Campbell, A., 1145
Mortimer, C. T. See Cass, R. C., 958
Moussa, A. A., Sammour, H. M., and Ghaly, H. A., 1269
Mulholland, T. P. C. See Grove, John Frederick, 1236
Nagarajan, K. See Govindachari, T. R., 983
Narayanan, C. R. See Barton, D. H. R., 963
Naylor, P., Ramage, G. R., and Schofield, F., 1190
Ogden, C. P. See Orville-Thomas, W. J., 1047
Ogle, J. R. See Elmore, D. T., 1141
Olive, L. W. See Baker, W., 1007
O'Meara, D., and Richards, G. N., 1204
Orville-Thomas, W. J., Parsons, A. E., and Ogden, C. P., 1047
O'Sullivan, D. G. See Holt, S. J., 1217
Owen, L. N. See Ali, Md. E., 1066, 1074
Parsons, A. E. See Orville-Thomas, W. J., 1047
Periam, J. D. See Barker, C. C., 1077
Peters, D., 1023, 1028, 1039
Porter, M. R. See Mathieson, A. R., 1298, 1301
Prevedorou, C. C. A. See Bradley, D. C., 1010

Pryke, J. M. See Badger, G. M., 1179
Quincey, P. G. See Cass, R. C., 958
Rajappa, S. See Govindachari, T. R., 1306
Ramadas, C. V. See Govindachari, T. R., 983
Ramage, G. R. See Naylor, P., 1190
Randall, E. W., and Sutton, L. E., 1266
Reid, D. H., Stafford, W. H., and Stafford, W. L., 1118
Reid, D. H., Stafford, W. H., Stafford, W. L., McLennan, G., and Voigt, A., 1110
Reid, D. H., Stafford, W. H., and Ward, J. P., 1100
Richards, G. N. See Machell, G., 1199, and O'Meara, D., 1204
Rodda, H. J. See Badger, G. M., 1179
Rogers, V. See Baker, W., 1007
Rose, F. L. See Hendry, J. A., 1134
Rossotti, F. J. C., and Rossotti, H. S., 1304
Rossotti, H. S. See Rossotti, F. J. C., 1304
Rust, R. A. See Ford, M. C., 1297
Sadler, P. W. See Holt, S. J., 1217
Salmon, J. E., and Wall, J. G. L., 1128
Sammour, H. M. See Moussa, A. A., 1269
Schlögl, K. See Ashworth, P. J., 950
Schofield, F. See Naylor, P., 1190
Schofield, K., 1312
Schofield, K. See also Keene, B. R. T., 1080
Selleck, M. E. See Ansell, M. F., 1167
Short, W. F. See Bartram, C. A., 1158
Skattebøl, L. See Jones, E. R. H., 1054
Springall, H. D. See Cass, R. C., 958
Stafford, W. H. See Reid, D. H., 1100, 1110, 1118
Stafford, W. L. See Reid, D. H., 1110, 1118
Sutton, L. E. See Bax, C. M., 1254, 1258, and Randall, E. W., 1266
Swanwick, J. D. See Bradley, D. C., 1010
Tatlow, J. C. See Bourne, E. J., 1274
Taylor, D. A. H. See Howell, F. H., 1248
Taylor, T. J. See Hough, L., 1212
Terrey, H., and Thabit, J., 1303
Thabit, J. See Terrey, H., 1303
Thomas, D. A. See Ansell, M. F., 1163
Thomas, G. H. S. See Hough, L., 1212
Thompson, J. M. See Ashworth, P. J., 950
Thomson, R. H. See Hardie, R. L., 1286
Tivey, D. J. See Campbell, A., 1145, and Davey, W., 1230
Tomkinson, J. C., and Williams, R. J. P., 1153
Turner, A. F. See Haworth, R. D., 1240
Voigt, A. See Reid, D. H., 1110
Wall, J. G. L. See Salmon, J. E., 1128
Walpole, A. L. See Hendry, J. A., 1134
Ward, J. P. See Reid, D. H., 1100
Wardlaw, W. See Bradley, D. C., 1010
Wassermann, A., 1014
White, A. W. See Campbell, I. G. M., 1184
Whiting, M. C. See Ashworth, P. J., 950, and Jones, E. R. H., 1054
Williams, R. J. P. See Tomkinson, J. C., 1153
Willicks, W. See Clar, E., 942
Woods, B. M. See Hough, L., 1212

# PAPERS ACCEPTED

Experiments on the synthesis of substances related to the sterols. Part LIV. Degradative and synthetical studies on the A-ring of androst-4-ene-3 : 17-dione. By M. J. TEMPLE ROBINSON

The stereochemistry of some 1 : 5-diaza*cyclo*octane derivatives. By R. KOLINSKI, (MISS) H. PIOTROWSKA, and T. URBANSKI

The relationship between proton dissociation constants and the stability constants of complex ions. By J. G. JONES, J. B. POOLE, J. C. TOMKINSON, and R. J. P. WILLIAMS

The oxidation-reduction potentials of complex ions. By J. C. TOMKINSON and R. J. P. WILLIAMS

Structure of aegelin. By R. N. CHAKRAVARTI and B. DASGUPTA

Deuterium isotope and solvent effects in the base-catalyzed keto–enol transformation of methylacetylacetone. By F. A. LONG and D. WATSON

Urea and related compounds. Part V. Some sulphenylthioureas. By FREDERICK KURZER and W. TERTIUK

The mechanism of the coupling of diazonium salts with heterocyclic compounds. Part III. Indazole. By R. D. BROWN, B. A. W. COLLER, and (in part) M. L. HEFFERNAN

The synthesis of 2 : 4′-dipridyl and some derivatives. By R. F. HOMER

Homologous 9-anthryl-1′-naphthylalkanes and a new carbon–carbon cleavage occurring during reduction by lithium aluminium hydride. By PETER RONA and URI FELDMAN

Pyridine-4-sulphonic acid. By A. M. COMRIE and J. B. STENLAKE

The synthesis of 2-*O*-β-D-xylopyranosyl-L-arabinose and its isolation from the partial hydrolysis of esparto hemicellulose. By G. O. ASPINALL and R. J. FERRIER

The chemistry of fungi. Part XXXI. The structure of rosenonolactone. By ADELAIDE HARRIS, ALEXANDER ROBERTSON, and W. B. WHALLEY

The chemistry of fungi. Part XXXII. Rosololactone, a metabolite of *Trichothecium roseum* Link. By ADELAIDE HARRIS, ALEXANDER ROBERTSON, and W. B. WHALLEY

The chemistry of fungi. Part XXXIII. The oxidation of sclerotioramine and the structure of sclerotiorin. By H. C. FIELDING, ALEXANDER ROBERTSON, R. B. TRAVERS, and W. B. WHALLEY

The chemistry of fungi. Part XXXIV. Rotiorin, a metabolite of *Penicillium sclerotiorum* van Beyma. By G. B. JACKMAN, ALEXANDER ROBERTSON, R. B. TRAVERS, and W. B. WHALLEY

Raman spectra and constitution of fused gallium dibromide. By L. A. WOODWARD, N. N. GREENWOOD, J. R. HALL, and I. J. WORRALL

Studies in the steroid group. Part LXXI. The preparation and reactions of 9α-methylergostane derivatives. By E. R. H. JONES, G. D. MEAKINS, and J. S. STEPHENSON

Urethane phosphate: synthesis and hydrolytic studies. By A. LAPIDOT and M. HALMANN

Formyl compounds. Part II. By URSULA M. BROWN, P. H. CARTER, and MURIEL TOMLINSON

Acidity dependence of cumene hydroperoxide decomposition. By A. W. DE RUYTER VAN STEVENINCK

Cyclic amidines. Part VII. Preparation of benziminazoles from *N*′-aryl-*N*-hydroxyamidines. By M. W. PARTRIDGE and H. A. TURNER

Synthesis of nucleoside-5′ pyrophosphates. By A. M. MICHELSON

*N*-Oxides and related compounds. Part XII. Infrared spectra of some carbonyl compounds. By A. R. KATRITZKY, A. M. MONRO, and (in part) J. A. T. BEARD, D. P. DEARNALEY, and N. J. EARL

The stereochemistry of molecules containing the N=C=N group: the structure of the monomethiodide of bis-*p*-dimethylaminophenylcarbodi-imide. By J. J. DALY and P. J. WHEATLEY

The ultraviolet adsorption spectra and stability constants of cuprous cyanide complexes. By E. A. SIMPSON and GWYNETH M. WAIND

Potential–pH dependence of the bismuth electrode in and out of contact with air. By H. M. SAMMOUR and A. A. MOUSSA

The heat of formation of nickel carbonyl from combustion calorimetry. By K. W. SYKES

Purines, pyrimidines, and glyoxalines. Part IX. Syntheses of uridine, 2-thiouridine, and some related compounds. By G. Shaw, R. N. WARRENER, and (in part) (MISS) M. H. MAGUIRE and R. K. RALPH

The configuration of adrenaline and of its *p*-hydroxyphenyl analogue. By P. PRATESI, A. LA MANNA, A. CAMPIGLIO, and V. GHISLANDI

XUM

*trans-cyclo*Heptane-1 : 2-dicarboxylic acid and its conversion into *trans-bicyclo*[5 : 3 : 0]decan-9-one. By D. C. Ayres and R. A. Raphael
The constituents of natural phenolic resins. Part XXIV. A synthesis of galgravin. By J. G. Blears and R. D. Haworth
Studies in the polyene series. Part LIII. The synthesis of *pseudo*cumyl analogues of β-ionone and vitamin A acid. By G. Lowe, F. G. Torto, and B. C. L. Weedon
The aporphine series. Part IV. The synthesis of (±)-stephanine. By D. H. Hey and Ather Husain
Homolytic aromatic substitution. Part XIII. The reaction of benzoyl peroxide with naphthalene. By D. I. Davies, D. H. Hey, and Gareth H. Williams
Homolytic aromatic substitution. Part XIV. Ratio of isomerides formed in the arylation of nitrobenzene with *p*-chlorophenyl and *n*-bromophenyl radicals. By Chang Shih, D. H. Hey, and Gareth H. Williams
Synthetical studies on terpenoids. Part I. The synthesis of squalene. By D. W. Dicker and M. C. Whiting
Studies in the xanthone series. Part II. Preparation and reactions of 1-formyl-2-hydroxyxanthone. By (the late) J. S. H. Davies, F. Lamb, and H. Suschitzky
An alternative synthesis of adenosine-2′(3′) : 5′ diphosphate. By A. M. Michelson
The constitutions of geodin and erdin. By D. H. R. Barton and A. I. Scott
1 : 12-2 : 3-10 : 11-Tribenzoperylene. By E. Clar and M. Zander.
Some new sulphur-containing diacids. By W. A. W. Cummings
Some new polycyclic derivatives of fluorene and carbazole. By G. Saint-Ruf, Ng. Ph. Buu-Hoï, and P. Jacquignon
The identity of gleditsin and mollisacacidin. By J. W. Clark-Lewis and N. Mitsuno
Some derivatives of *iso*pentylbenzene. By W. E. Harvey
Thiophen derivatives. Part XII. Some derivatives of 2-ethylthiophen. By Ng. Ph. Buu-Hoï
Amino-sugars and related compounds. Part IV. Acid reversion of 2-acetamido-2-deoxy-D-glucose (*N*-acetyl-D-glucosamine). By A. B. Foster and D. Horton
Derivatives of acetoacetic acid. Part IX. The reaction of diketen with carbodi-imides. By R. N. Lacey and W. R. Ward
The oxidation of the trisdipyridylosmium(II) ion by the peroxydisulphate ion in aqueous solution. By D. H. Irvine
Decahydro*iso*quinolines and related compounds. Part II. Some further examples of abnormal ultraviolet adsorption. By C. B. Clarke and A. R. Pinder
Some 2-substituted linear naphthiminazoles. By D. J. Brown
The solubility of arsenious oxide in aqueous hydrochloric acid at 25°. By I. A. Menzies and L. W. Owen
Tocopherols. Part II. Synthesis of tocol. By P. Mamalis, D. McHale, J. Green, and S. Marcinkiewicz
*cyclo*Hexane-1 : 3-diones. Part IV. The synthesis of further terphenyl derivatives. By G. R. Ames and W. Davey
*pseudo*Azulenes. Part I. Some derivatives of *cyclo*penta[b]pyran. By G. V. Boyd
Synthesis of mycolipenic acid. By D. J. Millin and N. Polgar
*N*-Oxides and related compounds. Part XIII. Infrared spectra of 4-substituted pyridine 1-oxides. By A. R. Katritzky and J. N. Gardner
Infrared studies of heterocyclic compounds. Part I. 4-Substituted pyridines. By A. R. Katritzky and J. H. Gardner
Immunopolysaccharides. Part IX. The enzymic synthesis of trisaccharides containing the α-1 : 2-glucosidic linkage. By R. W. Bailey, S. A. Barker, E. J. Bourne, P. M. Grant, and M. Stacey
Purines, pyrimidines, and glyoxalines. Part X. Synthesis of uracil 6-phosphonic acid. An analogue of orotic acid. By (Miss) M. H. Maguire, R. K. Ralph, and G. Shaw
The preparation and donor properties of some silylamines. By E. A. V. Ebsworth and H. J. Emeléus

## 185. *The Thermal Decomposition of* 3 : 5-*Dibromobenzene*-1 : 4-*diazo-oxide.*

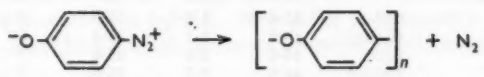
By M. J. S. Dewar and A. N. James.

3 : 5-Dibromobenzene-1 : 4-diazo-oxide decomposes in chlorobenzene above 70° to give nitrogen, bromine, and thermally stable polymers. These appear to be copolymers of bromochlorodiphenylyloxy- and dibromophenoxy-units. The mechanism of the reaction is discussed in terms of diradical intermediates and radical substitutions.

This paper describes part of a programme directed to the synthesis of polymers stable to heat. In view of the known thermal stability of diphenyl ether, it seemed to us that polyphenylene oxides might be of interest if they could be suitably synthesised.

In preliminary work we prepared polymers of this type from sodium *m*- and *p*-halogenophenoxides; the conditions required were, however, drastic, and the polymers were less stable than we expected. It seemed likely that the drastic conditions had led to side-reactions and introduction of labile groups into the polymers. We therefore sought a less violent synthesis.

One possibility seemed to be the thermal decomposition of benzene-1 : 4-diazo-oxides:



Reactions of this type have been observed in the photochemical decomposition of various solid diazo-oxides by Süss, Müller, and Heiss,[1] but the thermal decompositions have been little studied. Vaughan and Phillips [2] examined the thermal decomposition of various nitrobenzenediazo-oxides, but without sufficiently characterising the products.

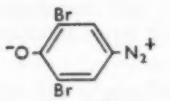
To avoid side reactions it was necessary to block the reactive positions *ortho* to oxygen in the diazo-oxide; we therefore worked with the 3 : 5-dibromo- and the 3 : 5-dichloro-derivative which are easily prepared, relatively stable, and have both *ortho*-positions blocked. For safety we used solutions of the diazo-oxides, although Süss *et al.* found the photolysis of diazo-oxides dissolved in aromatic solvents to follow a different course to that in the solid state; they obtained *p*-arylphenols in which molecules of solvent had replaced the diazo-group. The need for caution was, however, shown by an accident in which 70 g. of diazo-oxide detonated on gentle rubbing.

3 : 5-Dibromobenzene-1 : 4-diazo-oxide (I) was prepared fairly pure by Böhmer's method,[3] and its solutions in chlorobenzene decomposed smoothly at >70°. The theoretical amount of nitrogen was evolved, together with much free bromine, and deep red solutions were formed from which we isolated polymers, a little *s*-tribromophenol, and tar. The polymers sintered at 200—220°, were soluble in benzene, chloroform, or bromoform, and insoluble in alcohol, acetone, or light petroleum, and their molecular weights lay in the range 1600—3600. They were unaffected by strong acids or alkalis and by reducing agents, but they were attacked by strong oxidising agents. Analysis showed them to contain both chlorine and bromine, indicating that solvent molecules had been incorporated; this was confirmed by oxidative degradation to *p*-chlorobenzoic acid.

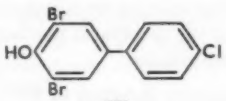
Treating the polymers with alkali or reducing agents failed to give definite products; but an indication of their structure was provided when the diazo-oxide was decomposed in chlorobenzene containing 1% of methanol or water. Under these conditions the yield of polymer was greatly reduced, and considerable quantities of phenols of lower molecular weight were formed. In addition to *s*-tribromophenol, two new isomeric phenols

[1] Süss, Müller, and Heiss, *Annalen*, 1956, **598**, 123.
[2] Vaughan and Phillips, *J.*, 1947, 1560.
[3] Bohmer, *J. prakt. Chem.*, 1881, **24**, 453.

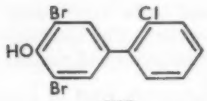
$C_{12}H_7OClBr_2$ were isolated. The work of Süss *et al.*[1] suggested very strongly that these were derivatives of 2 : 6-dibromophenol with a chlorophenyl group in the 4-position. We, therefore, synthesised 3 : 5-dibromo-4′-chloro-4-hydroxydiphenyl (II) by standard methods, and found it to be identical with one of the two phenols from our reaction; the isomeric phenol was presumably the 2′-chloro-isomer (III) since it gave *o*-chlorobenzoic acid on oxidation.



(I)



(II)



(III)

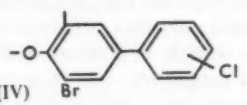
These results suggested that analogous diphenyl units might be present in the polymer. Table 1 shows the analyses of polymers prepared by heating (*B*) homogeneous solutions of the diazo-oxide and (*A*) a mixture of excess of solid diazo-oxide with the saturated solution; the calculated figures refer to a copolymer of (IV) and (V) in the proportions indicated in the last column. The agreement between calculated and observed figures is

TABLE 1. *Composition (%) of polymers formed under various conditions.*

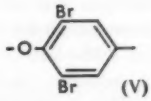
| | Conditions | | C | H | Br | Cl | O | (IV) (%) |
|---|---|---|---|---|---|---|---|---|
| *A* | 27 hr./72° | Calc. | 45·6 | 1·8 | 37·3 | 9·1 | 5·9 | 75 |
| | | Found | 45·6 | 2·3 | 38·8 | 6·7 | 6·8 | |
| *A* | 4½ hr./85° | Calc. | 46·6 | 1·9 | 35·6 | 9·7 | 5·8 | 79 |
| | | Found | 46·6 | 2·3 | 38·5 | 7·1 | 6·7 | |
| *B* | 1 hr./110° | Calc. | 48·4 | 2·0 | 32·8 | 10·8* | 5·8 | 88 |
| | | Found | 48·4 | 2·6 | 31·6 | 10·4 | 6·3 | |
| *A* | 1 hr./110° | Calc. | 42·3 | 1·6 | 42·6 | 7·7 | 6·0 | 60 |
| | | Found | 42·3 | 2·0 | 43·9 | 4·5 | 6·4 | |
| *B* | 1 hr./131° | Calc. | 49·6 | 2·0 | 31·0 | 11·4 | 5·7 | 93 |
| | | Found | 49·6 | 2·5 | 30·8 | 9·9 | 6·6 | |
| *A* | 1 hr./131° | Calc. | 43·8 | 1·7 | 40·0 | 8·2 | 5·9 | 67 |
| | | Found | 43·8 | 2·2 | 37·1 | 8·6 | 6·8 | |
| *A* | 1 hr./131°; (+ 1% of MeOH) | Calc. | 41·8 | 1·6 | 43·2 | 7·1 | 6·0 | 58 |
| | | Found | 41·8 | 2·1 | 39·6 | 9·2 | 6·9 | |
| *B* | Dichlorodiazo-oxide 1 hr./95° | Calc. | 58·6 | 2·5 | — | 30·1 | 6·9 | * |
| | | Found | 58·6 | 3·4 | — | 31·2 | 6·7 | |

* Calc. for 94% of $C_{12}H_6OCl_2$.

reasonable considering that end-groups have been neglected although the molecular weights of the polymers were not very high. The only real discrepancy appears in the hydrogen analyses which are uniformly too high (see below).



(IV)



(V)

Similar results were obtained on thermal decomposition of 3 : 5-dichlorobenzene-1 : 4-diazo-oxide in chlorobenzene. Nitrogen and chlorine were evolved and polymers were obtained with analyses analogous to those from the dibromodiazo-oxide, together with a little *s*-trichlorophenol. An example is given in Table 1.

The rate of evolution of nitrogen from the oxide (I) was investigated at several temperatures. Plotting $\log V_\infty/(V_\infty - V_t)$ against $V_t$ gives two intersecting straight lines, one of which passes close to the origin (see Figure). The apparent presence of two first-order stages is not understood. The first-order rate constants and derived activation energies are shown in Table 2.

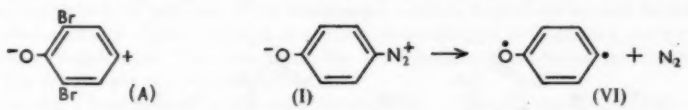
*Mechanism.*—The salient features of the reactions are the evolution of free halogen and the incorporation of molecules of solvent into the polymer. These suggest very

TABLE 2. *Rate constants and activation energies for the two stages in the decomposition of oxide* (I) *in chlorobenzene.*

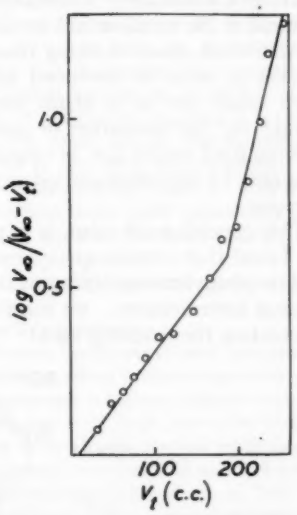
| Temp. | 72·3° | 78·2° | 81·3° | 90·5° | 101° | 110° |
|---|---|---|---|---|---|---|
| $10^4k_1$ (sec.$^{-1}$) | 1·55 | 3·43 | 5·61 | 12·1 | 31·7 | 70·8 |
| $10^4k_2$ (sec.$^{-1}$) | 4·08 | 8·75 | 8·31 | 12·1 | 19·7 | 22·8 |

$E_1 = 25$ kcal./mole. $E_2 = 11$ kcal./mole.

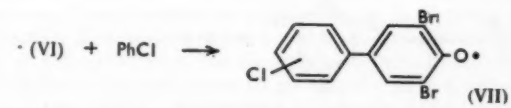
strongly that we are dealing with free-radical intermediates. Now loss of nitrogen from the diazo-oxide (I) might give a zwitterion (A) in which the + sign indicates that one $sp^2$-hybrid orbital of the ring carbon is empty. However, the binding energy of electrons attached to $C^+$ must be high, and the binding energy of the most weakly held π-electrons in the phenoxide ion low; it seems very likely, therefore, that particularly under non-polar




conditions, the diradical structure (VI) would be more stable than the zwitterion. This diradical is derived from the zwitterion by transference of one π-electron into the unshared $sp^2$-orbital of the *para*-carbon atom. Note that the zwitterion and the diradical (VI) are distinct and not components of a hybrid; they differ in symmetry, since the $sp^2$ carbon orbital is symmetric, and the π-orbitals are antisymmetric, with respect to the plane of the



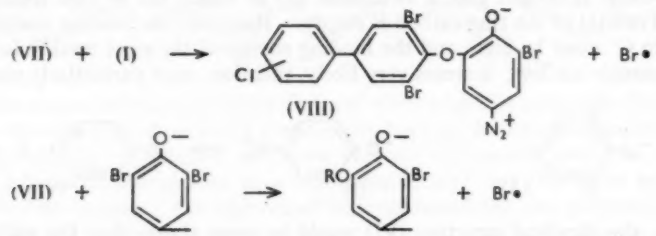

*Rate of decomposition of* 3 : 5-*dibromobenzene*-1 : 4-*diazo-oxide in chlorobenzene at* 72°.




ring. For the same reason there will be little coupling between the two unpaired electrons in the diradical, so it will behave as a genuine diradical.

Now the σ-radical centre in (VI) (*i.e.*, the odd electron in the $sp^2$ carbon atomic orbital) will not differ appreciably from that in a free phenyl radical; this centre should be extremely reactive, and in particular should be able to attack the solvent by radical substitution, giving a diphenylyloxy-radical (VII); formally a hydrogen atom would be evolved in this process, but in practice it would be expected to remain attached to the chlorophenyl ring; disproportionation would eventually give rise to products containing *cyclo*hexadiene systems—which would explain the high hydrogen contents recorded in Table 1.

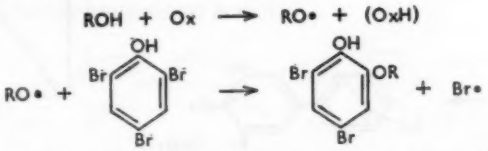
The other radical centre (π-radical centre) should be much less reactive, being analogous to that in the phenoxy-radical. Substitution into the solvent should therefore not occur here. However, radical displacement of bromine either from the diazo-oxide (I), or from a polymer molecule, should take place more readily, since the bromine should be somewhat activated by the adjacent oxygen atom and since C–Br bonds are relatively weak. In the former case a new diazo-oxide (VIII) will be formed, while the latter reaction is a propagation step in the growth of the polymer. In each case a bromine atom will be displaced, giving rise to the free bromine observed as a product of the reaction.




The inclusion of dibromophenoxy-units (V) in the polymer may be ascribed to coupling of the σ-radical centre of (VI), or the analogous diradical from (VIII), with the π-radical centres of monoradicals such as (VII) or of diradicals such as (VI). The formation of *s*-tribromophenol would arise from reaction of σ-radical centres with the free bromine formed in the reaction. Chains could be broken by reaction with the labile hydrogen atoms produced in the initial attack on the solvent.

Additional chain-breaking reactions could arise in the presence of water or methanol; reaction of water or methanol with free halogen would give rise to hydrogen bromide, which could act as a chain terminator: $RO\cdot + HBr \longrightarrow ROH + Br\cdot$. This would account for the formation of phenols of low molecular weight under these conditions. Bromine itself would not, of course, react effectively with radicals such as (VII); it could do so only by attacking carbon atoms in the phenoxide ring and so destroying its aromatic character.

This general mechanism is supported by the work of Hunter and his collaborators [4] who found that *s*-trihalogenophenols and related compounds were converted into polydihalogenophenylene oxides by oxidation. The mechanism which they suggested involved diradical intermediates; we consider it more likely that the mechanism is as follows, Ox representing the oxidising agent:




In confirmation we have found that free halogen is evolved in reactions of this type. We have also found that oxidation of 3 : 5-dibromo-4′-chloro-4-hydroxydiphenyl (II) gives polymers, the intermediate, according to our formulation, being the same radical (VII) that we postulate as an intermediate in the diazo-oxide decomposition.

## Experimental

**3 : 5-*Dibromobenzene*-1 : 4-*diazo-oxide*.**—The diazo-oxide was prepared according to Böhmer's directions [3] and dried before use. Recrystallisation from methanol did not alter the analysis or mode of decomposition significantly.

[4] Hunter *et al.*, *J. Amer. Chem. Soc.*, 1916, **38**, 1761; 1917, **39**, 2640; 1921, **43**, 131, 151; 1932, **54**, 1167.

3 : 5-*Dichlorobenzene*-1 : 4-*diazo-oxide*.—This *diazo-oxide* was prepared from the corresponding aminodichlorophenol by diazotisation, forming orange-brown needles (from methanol) exploding at 158° (Found: C, 38·9; H, 1·7; Cl, 37·5; N, 14·8. $C_6H_2ON_2Cl_2$ requires C, 38·1; H, 1·1; Cl, 37·5; N, 14·8%). Both compounds were dried over $P_2O_5$ *in vacuo* or by prolonged warming in an oven at 40°.

*Decompositions of Diazo-oxides*.—These were carried out on portions (2·78 g.) of compound (I) in varying quantities of chlorobenzene (fractionated from $P_2O_5$) in order to provide both heterogeneous and homogeneous conditions. Stirring was vigorous and temperature controlled. Bromine and solvent were removed at the water-pump, and the concentrated solutions were then filtered and poured into stirred methanol. The precipitated polymers were washed and dried at 100°, yielding 1·2—1·8 g. Evaporation of the methanol and extraction with alkali gave ~0·15 g. of *s*-tribromophenol, m. p. and mixed m. p. 96°

Bromine was estimated by sodium peroxide fusion of the polymer in a micro-Parr bomb, followed by oxidation of bromide to bromate with sodium hypochlorite and determination of bromate iodometrically. This method is a micro-modification of Haslam's macro-procedure.[5] Chlorine was calculated by difference from the total halide, thus giving an inherent error of ±10%. The results are shown in Table 1.

*Isolation and Identification of Phenolic By-products*.—The dibromodiazo-oxide (I) (139 g.) was decomposed in refluxing chlorobenzene (1 l.) containing methanol (10 c.c.). The polymer was removed in the usual way and the filtrate, after evaporation of the methanol, was extracted with alkali. The alkaline extracts were acidified and extracted with ether, and the ether extracts dried ($Na_2SO_4$) and evaporated. The phenolic residue was distilled, giving *s*-tribromophenol (12·2 g.), b. p. 120—124°/0·5 mm. The involatile residue was dissolved in hot alcohol, water was added, and later a large quantity of pink crystals was filtered off and recrystallised from benzene, to give three crops. The first crop, after repeated recrystallisation from alcohol and finally from light petroleum (b. p. 60—80°), gave almost white needles of 3 : 5-*dibromo*-4′-*chloro*-4-*hydroxydiphenyl*, m. p. 167·5—168·5° (Found: C, 39·9; H, 2·1; Br, 44·9; Cl, 10·9. $C_{12}H_7OClBr_2$ requires C, 39·8; H, 2·0; Br, 44·1; Cl, 9·8%); the *monomethyl ether*, prepared by diazomethane in ether, crystallised from alcohol in pale brown needles, m. p. 116·5—117·5° (Found: C, 40·2; H, 2·6; Br, 41·8; Cl, 10·2; OMe, 7·9. $C_{13}H_9OClBr_2$ requires C, 41·5; H, 2·4; Br, 42·5; Cl, 9·4; OMe, 8·2%). The second crop after several recrystallisations from aqueous alcohol and finally from light petroleum (b. p. 40—60°) gave slightly brown needles of 3 : 5-*dibromo*-2′-*chloro*-4-*hydroxydiphenyl*, m. p. 124—126° (Found: C, 39·6; H, 2·5; Br, 41·1; Cl, 9·8%), whose *monomethyl ether* crystallised from light petroleum (b. p. 40—60°) in white needles, m. p. 109—110° (Found: C, 41·2; H, 2·4; Br, 42·5; Cl, 9·4; OMe, 8·3%).

3 : 5-Dibromo-2′-chloro-4-hydroxydiphenyl with alkaline permanganate gave *o*-chlorobenzoic acid (10%), m. p. and mixed m. p. 138—139°.

The third crop of phenolic material did not yield any further product.

3 : 5-*Dibromo*-4′-*chloro*-4-*hydroxydiphenyl*.—4-Chloro-4′-methoxydiphenyl was prepared by the procedure used by Harley-Mason and Mann [6] for the corresponding bromo-compound. The crude ether fraction was distilled, under reduced pressure, through a column packed with glass helices. Two fractions were collected: (*a*) b. p. >140°/0·4 mm.; (*b*) b. p. 140—150°/0·4 mm. Fraction (*b*) deposited crystals which after recrystallisation from alcohol formed white needles, m. p. 110—111°, which on demethylation with hydrobromic acid in acetic acid and recrystallisation from light petroleum (b. p. 60—80°) gave 4′-chloro-4-hydroxydiphenyl, m. p. 145—146° (lit.,[7] 146—147°). Bromination of the phenol (1 g.) with bromine (1·76 g.) in carbon disulphide (10 c.c.) gave 3 : 5-dibromo-4′-chloro-4-hydroxydiphenyl, pale brown needles (0·8 g.) [from light petroleum (b. p. 60—80°)], m. p. 167·5—168·5° undepressed on admixture with the specimen prepared as above.

4′-*Chloro*-2-*methoxydiphenyl*.—Fraction (*a*) above, on crystallisation from methanol, gave prismatic needles, m. p. 50—52°, which by analogy with the work of Harley-Mason and Mann were assumed to be 4′-*chloro*-2-*methoxydiphenyl* (Found: C, 71·1; H, 5·1; OMe, 14·4. $C_{13}H_{11}OCl$ requires C, 71·4; H, 5·1; OMe, 14·2%).

Attempts to prepare 2′-chloro-4-methoxydiphenyl as a precursor of the phenol (III) from

[5] Haslam, *Analyst*, 1950, **75**, 371.
[6] Harley-Mason and Mann, *J.*, 1940, 1379.
[7] Angeletti and Gotti, *Gazzetta*, 1929, **58**, 630.

XUM

anisole and *o*-chloroaniline, gave only 2'-chloro-2-methoxydiphenyl, m. p. 53—54° (lit.,[8] 53—54°).

*Oxidation of Phenol* (III).—Heating the phenol (0·23 g.) with lead dioxide (0·5 g.) in dry benzene (30 c.c.) in presence of sodium sulphate (0·1 g.) under reflux for 2 hr., followed by filtration, concentration, and pouring into methanol, gave a pink *polymer* (0·16 g., 90%), sintering at 300° [Found: C, 50·9; H, 2·3; Br, 28·0; Cl, 14·0. $(C_{12}H_6OClBr)_n$ requires C, 51·2; H, 2·2; Br, 28·4; Cl, 12·6%].

*Measurements of Rates of Decomposition.*—Measurements were carried out in a flat-bottomed glass tube, 4 cm. in diameter, 17 cm. long, fitted with a glass-sheathed magnetic paddle. The tube was held in a thermostat-bath and connected to a conventional gas burette. Dry chlorobenzene (50 c.c.) was placed in the tube and brought to the required temperature. The stirrer was started, a weighed amount (0·3475 g.) of diazo-oxide (I) added rapidly, and the apparatus closed. First-order rate constants were calculated in the usual way from plots of the volumes of gas evolved.

QUEEN MARY COLLEGE,
MILE END ROAD, LONDON, E.1. [*Received, April 1st*, 1957.]

[8] Mascarelli and Pirora, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1937, **26**, 243.

---

## 186. *The Light Absorption of Pyrroles. Part I. Ultraviolet Spectra.*

By ULLI EISNER and P. H. GORE.

The ultraviolet light absorption of a number of pyrroles has been determined. The spectra are discussed, and correlations between structure and light absorption attempted.

THE ultraviolet light absorption of certain pyrroles has recently been reported,[1-5] but interpretation of the data has been scanty. The aim of the present contribution is to record some further light absorption data (see Table 1) and to establish a number of correlations. The work was initiated in 1952, so there is some duplication of our results with those of Cookson.[1]

Pyrrole itself possesses a strong band (*A*) in the 210 mμ region (ε 15,000),[6] and a weak one (band *B*) at 240 mμ (ε 300). Cookson [1] observed that alkyl-substitution lowered the intensity of band *A*, and caused band *B* to disappear. Six alkyl-substituted pyrroles (1—6) * have now been investigated, the hypochromic effect being confirmed. Band *B* is absent in the simple alkylpyrroles (1), (2), (3), but appears in the more complex compounds (4), (5), (6), shifted by up to 20 mμ towards the visible region. The spectra of the pyrrole–acetone (5) and pyrrole–butanone (6) adducts are in keeping with their structures, as recently confirmed by chemical evidence.[7]

A new band makes its appearance when the pyrrole nucleus is substituted by $-M$ substituents [compounds (7—42)]. There is also selective light absorption in region *B*,[1] *viz.*, ~250—270 mμ, but as the intensities are very much higher than those found for certain alkylpyrroles and pyrrole itself, it is likely that these maxima are here due to a new type of transition. This band is probably of normal *K*-type, because (i) it is present for all conjugated, and absent for non-conjugated, pyrroles, and (ii) the transition energy decreases (*i.e.*, $\lambda_{max.}$ shifts towards the visible region) with increasing conjugative powers

* These and similar numbers in parentheses refer to Tables.

[1] Cookson, *J.*, 1953, 2789.
[2] Andrisano and Pappalardo, *Gazzetta*, 1955, **85**, 1430.
[3] Bonino and Marinangeli, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1955, **19**, 222, 393.
[4] Scrocco and Nicolaus, *ibid.*, 1956, **20**, 795.
[5] Grob and Ankli, *Helv. Chim. Acta*, 1949, **32**, 2033; Grob and Camenish, *ibid.*, 1953, **36**, 49; Cookson and Rimington, *Nature*, 1953, **171**, 875; *Biochem. J.*, 1954, **57**, 476; Davoll, *J.*, 1953, 3802.
[6] Bowden, Braude, and Jones, *J.*, 1946, 948.
[7] Rothemund and Gage, *J. Amer. Chem. Soc.*, 1955, **77**, 3340.

TABLE 1. *Light absorption*[a] *of substituted pyrroles*

| | Subst. at position | | | | Band *A* | | Band *B* | | Band *K* | |
|---|---|---|---|---|---|---|---|---|---|---|
| No. | 2 | 3 | 4 | 5 | $\lambda_{max.}$ | ε | $\lambda_{max.}$ | ε | $\lambda_{max.}$ | ε |
| 1 | — | Et | Et | — | ~208 | 5900 | — | — | — | — |
| 2 | Me | — | Me | — | 218 | 4700 | — | — | — | — |
| 3 | Me[b] | Et | Me | — | 214 | 7000 | — | — | — | — |
| 4 | $CH_2{\cdot}NC_5H_{10}$ | Et | Et | — | 208 | 9200 | 270 | 40 | — | — |
| 5 | $Me_2C<$[c] | — | — | $Me_2C<$ | 219<br>227 | 4700<br>3700 | 280 | 110 | — | — |
| 6 | $MeEtC<$[c] | — | — | $MeEtC<$ | 227 | 4600 | 266<br>278 | 600<br>530 | — | — |
| 7 | $CO_2Et$ | Me | Me | — | — | — | — | — | 273 | 14,500 |
| 8 | $CO_2Et$[d] | Me | Me | Me | — | — | 253 | 6800 | 285 | 15,800 |
| 9 | $CO_2Et$[e,f] | Me | Me | $-CH_2-$ | — | — | — | — | 290 | 15,700 |
| 10 | $CO_2Et$[e] | Me | Et | $-CH_2-$ | — | — | — | — | 290 | 15,700 |
| 11 | $CO_2Et$ | Me | Me | $CH_2{\cdot}OMe$ | — | — | — | — | 271<br>282 | 15,000<br>17,500 |
| 12 | CH:N·OH | — | — | — | — | — | — | — | 272 | 17,600 |
| 13 | CHO[g] | — | — | — | — | — | 251 | 3100 | 287 | 13,300 |
| 14 | COMe[h,i] | — | — | — | — | — | 251 | 4100 | 290 | 16,400 |
| 15 | CH:CH·COMe | — | — | — | — | — | — | — | 352 | 16,900 |
| 16 | CH:CH·COPh | — | — | — | — | — | 262 | 9300 | 386 | 24,500 |
| 17 | Me | CN | — | Me | — | — | — | — | 246 | 5500 |
| 18 | Me[j] | $CO_2Et$ | Me | — | 232 | 9000 | — | — | 258 | 5300 |
| 19 | Me[k] | COMe | Me | — | 209 | 10,300 | 250 | 10,400 | 282 | 4900 |
| 20 | $CO_2Et$ | Me | Me | $CO_2Et$ | 220 | 16,700 | — | — | 282 | 22,000 |
| 21 | $CO_2Me$ | Et | Et | $CO_2Me$ | 222 | 17,700 | — | — | 282 | 19,800 |
| 22 | $CO_2H$ | Et | Et | $CO_2Et$ | 222 | 17,900 | — | — | 280 | 19,100 |
| 23 | $CO_2H$ | Et | Et | $CO_2H$ | 220 | 19,600 | — | — | 280 | 19,200 |
| 24 | COMe[k] | — | — | COMe | 229 | 12,800 | — | — | 305 | 16,400 |
| 25 | CHO[m] | Et | Et | $CO_2Et$ | 232 | 12,500 | — | — | 305 | 17,400 |
| 26 | $CO{\cdot}CO_2Me$[k] | — | — | $CO_2Me$ | 227 | 7500 | — | — | 312 | 13,200 |
| 27 | Me | CN | CN | Me | — | — | — | — | 252 | 8100 |
| 28 | Me | $CO_2Et$ | CN | Me | — | — | — | — | 262 | 9200 |
| 29 | — | $CO_2Et$ | $CO_2Et$ | — | 209 | 13,200 | — | — | 253 | 7500 |
| 30 | Me | CN | CH:N·OH | Me | — | — | 240 | 7500 | 280 | 9800 |
| 31 | Me | CHO | CN | Me | 222<br>227 | 11,000<br>10,800 | 255 | 8700 | 285 | 7400 |
| 32 | Me | $CO_2Et$ | CHO | Me | 232 | 11,300 | 264 | 6600 | 295 | 8000 |
| 33 | $CO_2Et$ | Me | $CO_2Et$ | Me | 221 | 27,500 | — | — | 273 | 16,700 |
| 34 | $CO_2Et$[n] | Me | $CO_2Et$ | Me | 226 | 29,100 | — | — | 274 | 14,400 |
| 35 | $CO_2Et$ | Me | $CO_2H$ | Me | 220 | 23,600 | — | — | 273 | 15,200 |
| 36 | $CO_2H$ | Me | $CO_2Et$ | Me | 220 | 24,100 | — | — | 271 | 15,200 |
| 37 | $CO_2Et$ | Me | $CO_2Et$ | $CHCl_2$ | 222 | 21,400 | — | — | 260 | 11,100 |
| 38 | $CO_2Et$[o] | Et | COMe | Me | 236 | 22,000 | — | — | 286 | 11,700 |
| 39 | $CO_2Et$ | Me | CHO | Me | 240 | 22,400 | — | — | 288 | 10,100 |
| 40 | Me | $CO_2Et$ | Me | CHO | 220<br>228 | 15,400<br>15,200 | — | — | 297 | 20,900 |
| 41 | $CO_2Et$ | Me | $CO_2Et$ | $CO_2Me$ | 224 | 24,000 | — | — | 276 | 17,500 |
| 42 | $CO_2Et$ | Me | $CO_2Et$ | CHO | 237 | 21,500 | 270 | 7600 | 308 | 11,100 |

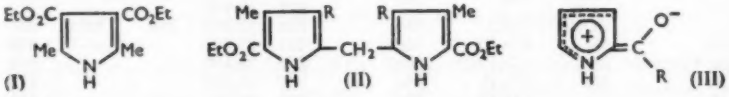
[a] In EtOH unless otherwise stated. [b] Cookson [1] gives $\lambda_{max.}$ ~200 mμ (ε 7450). [c] Pyrrole–ketone adducts; ε given per pyrrole unit. [d] In dioxan, $\lambda_{max.}$ 281 mμ (ε 16,400). [e] Dipyrrylmethane (II); ε given per pyrrole unit. [f] In dioxan, $\lambda_{max.}$ 287 mμ (ε 15,900). [g] Andrisano and Pappalardo [2] give $\lambda_{max.}$ ~252, 289·5; (ε 5000; 16,600). [h] In MeOH. [i] Andrisano and Pappalardo [2] give $\lambda_{max.}$ ~250, 287 mμ (ε 4400; 15,800). [j] Cookson [1] gives $\lambda_{max.}$ 232, 259 mμ (ε 8480; 5030). [k] Cookson [1] gives $\lambda_{max}$ <210, 251, 271—285 mμ (ε >10,000; 10,000; 4760). [l] Cf. ethyl 4-ethyl-5-methoxycarbonyl-3-methylpyrrole-2-carboxylate for which Cookson gives $\lambda_{max.}$ 221, 282 mμ (ε 17,700; 21,900). [m] Cf. ethyl 4-ethyl-5-formyl-3-methylpyrrole-2-carboxylate, for which Cookson gives $\lambda_{max.}$ 231, 303 mμ (ε 14,200; 21,100). [n] *N*-Methyl derivative. [o] Cf. ethyl 4-acetyl-3 : 5-dimethylpyrrole-2-carboxylate, for which Cookson gives $\lambda_{max.}$ 235, 283 mμ (ε 22,800; 11,800), with an inflection at 255 mμ (ε 12,000).

of substituents, *viz.*, in the approximate sequence $CN < CO_2H < CO_2R < CH{:}N{\cdot}OH <$ CHO ~COMe < $CO{\cdot}CO_2R$ < CH:CH·COMe < CH:CH·COPh (cf. ref. 2). For example, the absorption at longer wavelength of the compound (40), compared with that of the isomer (39), is clearly due to the predominating influence of the more strongly conjugating 2-formyl group. We find the difference between the $\lambda_{max.}$ values of $CO_2H$ and $CO_2R$ derivatives to be only about 2 mμ, compared with ~6 mμ previously reported.[2]

The *K*-band maxima are shifted by approximately 7 mμ towards the red region for each nuclear alkyl group (cf. refs. 1, 3), independently of the position of substitution. It appears possible that steric interference could take place between a bulky alkyl group and a vicinal chromophoric substituent.* This would reduce π-electron interaction between the substituent and the pyrrole nucleus, thus reducing the ε value, or, in extreme cases, producing a hypsochromic shift. In the related system of *o*-methyl-substituted benzaldehydes and acetophenones,[8] a reduction in ε was the only observed effect. In the pyrrole series a similar effect appears to take place. Thus replacement of the two nuclear methyl groups in the diester (20) by ethyl groups (21) reduces the ε value by 2200. Similarly comparison of the diester (29) with Cookson's pyrrole [1] (I), which contains two additional methyl groups, shows a lowering of ε by 950.

Pruckner and Dobeneck [9] have recorded values of 281 mμ for the dipyrrylmethanes (II; R = Me; compound 9) and (II; R = Et; compound 10) (in dioxan), a result which we considered rather too low. On repeating the measurements in ethanol, we found values of 290 mμ in each case [in dioxan compound (9) had $\lambda_{max.}$ 287 mμ]. The corresponding mononuclear trialkylpyrrole ester (8) had a maximum at 285 mμ (281 mμ in dioxan). Thus a bathochromic shift of 5—6 mμ occurs when two pyrrole units are separated by a methylene bridge, pointing to conjugation (in the excited state) across the methylene bridge equivalent to 1·7 kcal./mole.† Analogously there is evidence of electronic interaction in diphenylmethane [10] between the two benzene rings across the methylene bridge.

3-Substituted pyrroles absorb at shorter wavelengths (15—20 mμ) than the corresponding 2-derivatives. This indicates that conjugation in the excited state, with a resulting lowering of energy, is more pronounced in the latter, so that the absorption maximum occurs at longer wavelengths in the former. Calculations on two matched pairs of derivatives ‡ point to a difference in conjugation energy (in the excited states) of 6·0 and 6·1 kcal./mole, respectively. The differences in conjugation energy in the ground state of 2- and 3-derivatives are of the order of 2·5—3·0 kcal./mole, as determined by combustion methods.[11]




The relative conjugating power of the pyrrole, furan, and benzene nuclei may be compared by examining the $\lambda_{max.}$ values of the *K*-bands in, say, the corresponding 2-Ar·CH:CH·COMe derivatives. They are in the order of 2-pyrryl ($\lambda_{max.}$ 352 mμ) > 2-furyl ($\lambda_{max.}$ 310 mμ) [12] > phenyl ($\lambda_{max.}$ 285 mμ),[13] a sequence expected from the recorded data on chemical reactivity.

The nature of the *K*-band of pyrroledicarboxylic acids and esters is more complex (cf. ref. 4), as there appears to be no direct correlation between the energy of the *K*-type transition and the conjugation effects that can be predicted for the 2- and 3-positions. *A priori* it was considered unlikely that −*M* substituents would interact conjugatively

* Inspection of models shows that there would be more steric interference in the 2 : 3-positions than in the 3 : 4-positions.

† The calculated difference in energy between transitions occurring at 285 mμ and 290 mμ.

‡ Compounds (7) and (18); and 2-acetyl-4-ethyl-3 : 5-dimethylpyrrole for which Cookson [1] gives $\lambda_{max.}$ 308 mμ, and compound (19), corrected for a third alkyl group, *i.e.*, $\lambda_{max.}$ 289 mμ.

[8] Braude, Sondheimer, and Forbes, *Nature*, 1954, **173**, 117; Braude and Sondheimer, *J.*, 1955, 3754.

[9] Pruckner and Dobeneck, *Z. phys. Chem.*, 1941, **190**, *A*, 43.

[10] Braude, *J.*, 1949, 1902.

[11] Stern and Klebs, *Annalen*, 1932, **500**, 107; 1933, **504**, 296.

[12] Hughes and Johnson, *J. Amer. Chem. Soc.*, 1931, **53**, 737.

[13] Braude, *Ann. Reports*, 1945, **42**, 105.

with each other *via* the nucleus either in the ground or the transition state; thus the spectra of esters were expected for follow an additive scheme, *i.e.*, the sequence of increasing wavelengths: 3- < 3 : 4- < 2- < 2 : 3- and 2 : 4- < 2 : 5-. This order is approximately followed, as seen from Table 2 in which are listed $\Delta\lambda$ and $\Delta\varepsilon$ values of the various esters investigated. The 2- and the 3-carboxylic acids are used as a basis for comparison, together with values given by Scrocco and Nicolaus [4] for the acids.

It appears that further substitution of a $CO_2R$ group into a molecule containing an acid or an ester group lowers the transition energies of the *K*-band appreciably. This applies not only to $CO_2R$ groups, but to any $-M$ group, as seen from Table 1. Substitution of such a group will cause increased contributions from polar forms, such as (III) (*i.e.*, conjugation of one of the $-M$ substituents with the nucleus), in the excited state, thereby lowering its energy and decreasing the energy of the total transition.

This effect is remarkably powerful in the 2 : 3-derivatives which have very high $\lambda_{max.}$ values. It is striking that the introduction of further $CO_2R$ groups causes a distinct hypsochromic shift, which is most pronounced when the group enters the 5-position.

In all cases listed in Table 2, in which a $CO_2R$ grouping is being substituted in the

TABLE 2.[d]

Acids [a]

| Position substd. | $\lambda_{max.}$ | $\varepsilon$ | $\Delta\lambda_\alpha$ | $\Delta\varepsilon_\alpha$ | $\Delta\lambda_\beta$ | $\Delta\varepsilon_\beta$ |
|---|---|---|---|---|---|---|
| 2- | 262 | 12·0 | 0 | 0 | — | — |
| 3- | 245 | 4·8 | — | — | 0 | 0 |
| 2 : 3- | 282 | 4·2 | +20 | −7·8 | +37 | −0·6 |
| 2 : 4- | — | — | — | — | — | — |
| 2 : 5- | 272 | 20·1 | +10 | +8·1 | — | — |
| 3 : 4- | 259 | 7·3 | — | — | +14 | +2·5 |
| 2 : 3 : 4- | 279 | 8·0 | +17 | −4·0 | +34 | +3·2 |
| 2 : 3 : 5- | 270 | 10·3 | + 8 | −1·7 | +25 | +5·5 |
| 2 : 3 : 4 : 5- | 277 | 7·6 | +15 | −4·4 | +32 | +2·8 |

Ethyl esters [b,e]

| Position substd. | $\lambda_{max.}$ | $\varepsilon$ | $\Delta\lambda_\alpha$ | $\Delta\varepsilon_\alpha$ | $\Delta\lambda_\beta$ | $\Delta\varepsilon_\beta$ |
|---|---|---|---|---|---|---|
| 2- | 273 | 14·5 | 0 | 0 | — | — |
| 3- | 258 | 5·3 | — | — | 0 | 0 |
| 2 : 3- | 293 [c] | 10·5 | +20 | −4·0 | +35 | + 5·2 |
| 2 : 4- | 273 | 16·7 | 0 | +2·2 | +15 | +11·4 |
| 2 : 5- | 282 | 22·0 | + 9 | +7·5 | — | — |
| 3 : 4- | 267·5 [c] | 8·5 | — | — | + 9·5 | + 3·2 |
| 2 : 3 : 4- | — | — | — | — | — | — |
| 2 : 3 : 5- | 283 | 18·0 | +10 | +3·5 | +25 | +12·7 |
| 2 : 3 : 4 : 5- | — | — | — | — | — | — |

[a] Scrocco and Nicolaus.[4] [b] Present work unless otherwise stated. [c] The data extrapolated where necessary to two nuclear methyl groups, assuming that substitution of one methyl group produces $\Delta\lambda$ + 7 mμ and $\Delta\varepsilon$ + 500. [d] $\Delta\lambda_\alpha$, $\Delta\varepsilon_\alpha$ represent the increase, respectively, of $\lambda_{max.}$ (mμ) and $\varepsilon \times 10^{-3}$, of the substance over the parent 2-derivative; $\Delta\lambda_\beta$, $\Delta\varepsilon_\beta$ refer to the corresponding values compared to those of 3-derivative. $\varepsilon$ values to be multiplied by $10^3$. [e] Ref. 1.

3-position next to a 2-$CO_2R$ group already present, a sharp reduction in $\varepsilon$ is observed. Since normally a bathochromic displacement of a *K*-band is accompanied by an increase in the $\varepsilon$ value, this effect must be due to appreciable hindrance between the $CO_2R$ groups, causing displacement from coplanarity (or angular displacement) similar to those referred to above.

From a careful examination of the various types of pyrroles substituted with $-M$ groups, a regular pattern may be seen, *viz.*, that the $\varepsilon$ values are very largely, though not exclusively, governed by the positions of substitution rather than by the type of substituent, a phenomenon not observed in, say, the benzene system. The orders of magnitude of $\varepsilon$ values shown by substituted pyrroles have been collated in Table 3, and should be of use in determining structural details of pyrrole derivatives. Thus, for example, during

XUM

other work, the preparation [14] of diethyl 5-formyl-3-methylpyrrole-2 : 4-dicarboxylate (42) was repeated. It is now shown that, under the conditions specified, the corresponding 2-dichloromethyl derivative (37), having the same m. p. as the aldehyde, is not hydrolysed, contrary to the findings of previous workers. Its ultraviolet absorption was quite different from that expected for the 2-formyl derivative (42). The latter may be formed under more vigorous hydrolytic conditions, and its light absorption is in agreement with data given in Table 2 and 3.

TABLE 3. *Range of* ε *values* ($\times 10^{-3}$) *for pyrrole derivatives substituted by* —*M groups*

| | Band *A* | Band *B* | Band *C* | | Band *A* | Band *B* | Band *C* |
|---|---|---|---|---|---|---|---|
| 2- ..... | — | 5—9 * | 13—20 | 2 : 5- ..... | 12—20 | — | 17—22 |
| 3- ..... | 8—10 | 10 * | 4—5 | 2 : 3- ..... | 8—12 | 4—6 * | 10—12 |
| 3 : 4- ..... | 11—13 † | 6—8 * | 7—10 | 2 : 3 : 5- ..... | 21—24 † | 7—10 † | 9—17 |
| 2 : 4- ..... | 20—25 | 10—12 * | 10—17 | | | | |

* Or submerged. † Or absent.

[*Added, January 8th*, 1958.—Further ultraviolet data for pyrrolecarboxylic acid and esters were presented recently.[14a] A case of 3 : 4-interaction is given in that 4-methyl substitution in ethyl pyrrole-3-carboxylate gave a hypsochromic shift of 13 mμ. The effect on extinction coefficients was not reported.]

## EXPERIMENTAL

The spectroscopic measurements were carried out on a Unicam S.P. 500 spectrophotometer; some preliminary results were obtained on a Hilger-Spekker spectrophotometer.

*Preparation of Pyrroles.*—Unless otherwise stated, the pyrroles were prepared by the standard methods due to Fischer.[15] The methods for preparing the remaining pyrroles have been recorded in the following publications: compounds (8), (20), (35), (39), Eisner *et al.*; [16] compounds (1), (4), (21), (22), (23), (25), (38), Eisner *et al.*; [17] compounds (17), (27), (28), (30), (31), (32), Bilton and Linstead; [18] compound (29), Kornfeld and Jones; [19] compound (7), Kleinspehn; [20] compound (40) by a modification of the method of Chu and Chu; [21] compound (41), Corwin *et al.*; [14] compounds (5), (6), Rothemund and Gage; [7] compound (16), Ross and Waight.[22] They were purified to constant m. p. by crystallisation and sublimation under reduced pressure, or by distillation where appropriate.

The esters (18) [15] and (34) [22] were purified by chromatography on alumina with benzene–light petroleum (b. p. 60—80°) (1 : 1) as eluant.

*Diethyl 3-Dichloromethyl-5-methylpyrrole-2 : 4-dicarboxylate* (37).—The method of Corwin *et al.*[14] for the preparation of diethyl 3-formyl-5-methylpyrrole-2 : 4-dicarboxylate (42) was followed. The solid isolated, after recrystallisation and sublimation under reduced pressure, had m. p. 124°, and gave a positive Beilstein test. Elementary analysis indicated that it was the dichloromethyl derivative (37) (Found: C, 47·6; H, 5·2; N, 4·6. Calc. for $C_{12}H_{15}O_4NCl_2$: C, 46·8; H, 5·1; N, 4·55%). It was boiled with aqueous alcohol for 3 hr., which converted it into the aldehyde (42), m. p. 126°, after crystallisation from aqueous alcohol (Found: C, 57·4; H, 6·2. Calc. for $C_{12}H_{15}O_5N$: C, 56·9; H, 6·0%). A mixture of the two substances melted at 95°.

*Ethyl 5-Methoxymethyl-3 : 4-dimethylpyrrole-2-carboxylate* (11).—To the ester (8) (3·75 g.) in "AnalaR" acetic acid (120 c.c.) lead tetra-acetate (9·19 g.) was added during 1 hr. The solution was stirred at room temperature for 1·5 hr., the solvent removed under reduced pressure (<60°), and the residue dissolved in chloroform and washed with water until free from lead salts. The

[14] Corwin, Bailey, and Viohl, *J. Amer. Chem. Soc.*, 1942, **64**, 1267.
[14a] Scrocco and Nicolaus, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1957, **22**, 311, 500.
[15] Fischer–Orth, "Die Chemie des Pyrrols," Akademische Verlag Gesellschaft, Leipzig, 1937, Vol. I.
[16] Eisner, Linstead, Parkes, and Stephen, *J.*, 1956, 1655.
[17] Eisner, Lichtarowicz, and Linstead, *J.*, 1957, 733.
[18] Bilton and Linstead, *J.*, 1937, 922.
[19] Kornfeld and Jones, *J. Org. Chem.*, 1954, **19**, 1671.
[20] Kleinspehn, *J. Amer. Chem. Soc.*, 1955, **77**, 1546.
[21] Chu and Chu, *J. Org. Chem.*, 1954, **19**, 266.
[22] Ross and Waight, unpublished results.
[23] Corwin and Quattlebaum, *J. Amer. Chem. Soc.*, 1936, **58**, 1083.

solution was dried, the solvent removed, and the residue crystallised from aqueous methanol, affording a small amount of an impure solid, m. p. 158—178°, and a filtrate A. The solid was sublimed at 120°/20 mm., affording a sublimate, m. p. 69—72°, and a residue which after crystallisation from ethanol had m. p. 196—198°. It was identified as the dipyrrylmethane (9) (Found: C, 65·7; H, 7·7; N, 7·95. Calc. for $C_{19}H_{26}O_4N_2$: C, 65·9; H, 7·6; N, 8·1%). The filtrate A was diluted with water and extracted with chloroform. Removal of the solvent under reduced pressure and crystallisation from light petroleum (b. p. 60—80°) afforded *ethyl 5-methoxymethyl-3 : 4-dimethylpyrrole-2-carboxylate*, which after sublimation at 80°/20 mm. had m. p. 68—70° (Found: C, 62·5; H, 8·3; N, 6·7; OMe, 34·7. 34·6. $C_{11}H_{17}O_3N$ requires C, 62·5; H, 8·1; N, 6·6; OMe, 36·9%).

We are indebted to Dr. R. P. Linstead, C.B.E., F.R.S., for a gift of pyrroles (17), (27), (28), (30), (31), (32); to Dr. J. A. Elvidge for pyrroles (14), (24), (26); to Dr. E. Waight for compound (16); and to Mrs. I. Boston for the spectroscopic measurements. The work was carried out with the financial support from the Rockefeller Foundation to whom thanks are offered.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
SOUTH KENSINGTON, LONDON, S.W.7.
ACTON TECHNICAL COLLEGE, HIGH STREET, ACTON,
LONDON, W.3.
BOROUGH POLYTECHNIC, BOROUGH ROAD,
LONDON, S.E.1.

[*Received, July 11th*, 1957.]

---

## 187. *Infrared Spectra and Crystallinity. Part V.* Dimethyl and Diethyl Esters of αω-Dicarboxylic Acids.*

By P. J. CORISH and W. H. T. DAVISON.

Infrared spectra of liquid and crystalline dimethyl and diethyl alkanedicarboxylates, $[CH_2]_n(CO_2R)_2$ (where $n = 2$—8, 10, 14) have been measured from 3500 to 670 cm.$^{-1}$.

The spectra of the liquids are blurred but some bands appear which do not occur in the spectra of the crystals. These are probably due to non-*trans*-configurations of the $[CH_2]_n$ chain. In the crystalline state, however, bands are sharper and several new bands appear, mostly in the 1000—700 cm.$^{-1}$ region. These are attributed for the most part to an approximately *trans*-configuration of the $[CH_2]_n$ chain.

PREVIOUS work on polyesters,[1] di-[2] and mono-carboxylic[3] acids, paraffins,[4-6] and alkyl[6] and polymethylene halides[7-11] has established that spectral differences are generally observed between liquid and crystalline states of aliphatic compounds containing a $[CH_2]_n$ chain (where $n \geqslant 2$).

This investigation extends the work on dicarboxylic acids[2] to the dimethyl and diethyl esters.

### EXPERIMENTAL

The esters examined were either good-quality commercial materials which were redistilled if the b. p.s differed appreciably from literature values, or were prepared on a semimicro-scale from the appropriate acid and alcohol (fluorosulphuric acid being used as catalyst). Distillation

* The Infrared Spectra of Some Monocarboxylic Acids, *J.*, 1957, 1746, is regarded as Part IV.

[1] Davison and Corish, *J.*, 1955, 2428.
[2] Corish and Davison, *ibid.*, p. 2431.
[3] Corish and Chapman, *J.*, 1957, 1746.
[4] Brown, Sheppard, and Simpson, *Discuss. Faraday Soc.*, 1950, **9**, 261.
[5] Sheppard and Simpson, *Quart. Reviews*, 1953, **7**, 19.
[6] Brown, Sheppard, and Simpson, *Phil. Trans.*, 1954, *A*, **247**, 35.
[7] Brown and Sheppard, *Discuss. Faraday Soc.*, 1950, **9**, 144.
[8] *Idem, Trans. Faraday Soc.*, 1954, **50**, 535.
[9] *Idem, ibid.*, p. 1164.
[10] *Idem, ibid.*, 1952, **48**, 128.
[11] *Idem, Proc. Roy. Soc.*, 1955, *A*, **231**, 555.

or recrystallisation until constant spectra were obtained yielded products with b. p.s or m. p.s in good agreement with the literature (see Table 4).

Spectroscopic measurements were made with a Grubb-Parsons S.3 spectrometer (with sodium chloride prism) and a D.B.1 double-beam radiation unit.

Spectra of crystals of the esters normally liquid at, or just above, room temperature were obtained in a transmission type " cold cell ",[3] solid carbon dioxide–alcohol being used as refrigerant.

The spectra of esters solid at room temperature were measured by the potassium chloride disc technique; by heating the discs just above the m. p. of the ester in a " hot cell," [1, 2] the spectra of the molten state were obtained. After the diesters had recrystallised, the spectra were re-measured to check that no decomposition had occurred.

## Discussion

The previously reported [1-11] spectra of molecules containing a $[CH_2]_n$ chain fall into two main classes: (*a*) Those which have more bands in the liquid-state spectra and fewer in the crystalline-state spectra, *e.g.*, paraffins, alkyl halides, and polymethylene halides; [4-11] only one configuration, the most energetically stable, which is usually *trans*, exists in the solid, and this and other rotational isomers exist in the liquid. (*b*) Those which have more and sharper bands in the crystalline-state spectra and fewer and more blurred bands in the liquid-state spectra, *e.g.*, polyesters,[1] di- [2] and mono- [3] carboxylic acids, and glycols.[12] The *trans*-configuration usually occurs in the solid, and the absence of sharp bands in the liquid is attributed to " non-discrete rotational isomerism." [2]

The general changes in spectra of the diesters on melting are similar to those observed in the polyesters [1] and dicarboxylic acids,[2] *i.e.*, a marked broadening of bands leading to similar spectra for adjacent members of the series. However, unlike the polyesters and dicarboxylic acids, the diesters (especially the lower members) show some additional bands in the liquid which are assigned to discrete non-*trans*-configurations. In this respect the diesters resemble the long-chain paraffins and dihalides.

The occurrence of non-discrete rotational isomerism has been attributed [2] to strong intermolecular forces which are comparable to the barriers to free rotation about the C–C bonds. The intermolecular forces in diesters due to interactions of strong permanent dipoles are intermediate in strength between the hydrogen bonding in dicarboxylic acids and the purely van der Waals forces in paraffins, and the observed spectra of the liquid diesters are consistent with a combination of discrete and non-discrete configurations.

The absorptions which only appear in spectra of liquids are less noticeable in spectra of the higher diesters, in which the number of possible rotational isomers is greater.

The spectra of the liquid and the crystalline diesters (from 1500 to 670 cm.$^{-1}$) are shown in Figs. 1—5, the absorptions of the corresponding crystalline acids [2] (other than the 930 cm.$^{-1}$ δOH absorption) being shown by crosses. It is evident that the spectra of the crystalline esters and acids are very similar, particularly in the region below 1000 cm.$^{-1}$, and this confirms the expected *trans*-configuration of the esters. Diethyl glutarate is an exception as its crystalline-state spectrum differs markedly from those of the corresponding methyl ester and acid. It is probable therefore that diethyl glutarate crystallises in a non-planar configuration.

Two different spectra of both dimethyl and diethyl pimelate were obtained under different conditions and are commented on later. The spectra which are thought to be more representative of an all-*trans*-configuration are shown in Fig. 2.

C–H *Stretching Vibrations* (3050—2800 cm.$^{-1}$).—No pronounced differences occur between spectra of the crystalline and the liquid diesters except that, in the former, the bands are sharper. As a lithium fluoride prism was not used for this region no attempt will be made to report or interpret any small changes.

[12] Corish and Davison, to be published.

FIG. 1. FIG. 2. FIG. 3. FIG. 4.

*A.* Dimethyl succinate.
*B.* Diethyl succinate.
*C.* Dimethyl glutarate.
*D.* Diethyl glutarate.
*E.* Dimethyl adipate.
*F.* Diethyl adipate.
*G.* Dimethyl pimelate.
*H.* Diethyl pimelate.
*I.* Dimethyl suberate.
*J.* Diethyl suberate.
*K.* Dimethyl azelaate.
*L.* Diethyl azelaate.
*M.* Dimethyl sebacate.
*N.* Diethyl sebacate.
*O.* Dimethyl decamethylenedicarboxylate.
*P.* Diethyl decamethylenedicarboxylate.

In Figs. 1—5: —— = crystalline, - - - - = molten, and × indicates the corresponding bands for the dicarboxylic acids.

FIG. 5. FIG. 6. FIG. 7.

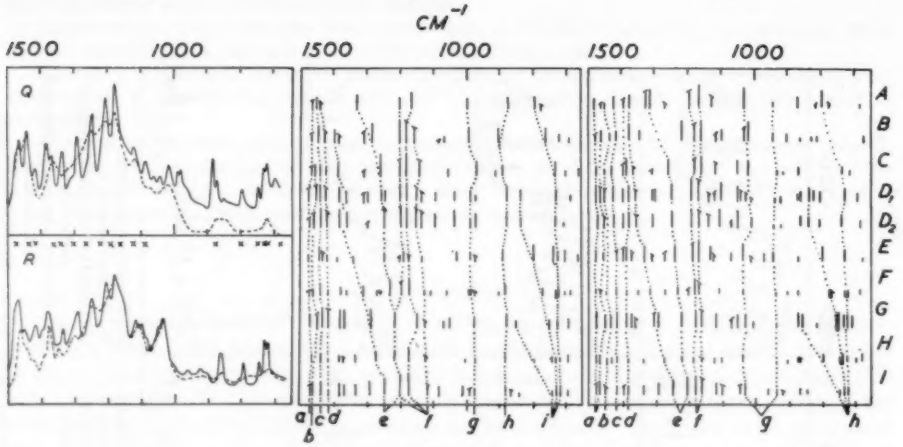



FIG. 5.

*Q*. Dimethyl thapsate (tetradecamethylenedicarboxylate).
*R*. Diethyl thapsate (tetradecamethylenedicarboxylate).

FIG. 6. *Dimethyl esters.*

*A*. Succinate.
*B*. Glutarate.
*C*. Adipate.
*D*. Pimelate { *D*1, tttt confign. / *D*2, tttg confign.
*E*. Suberate.
*F*. Azeläate.
*G*. Sebacate.
*H*. Decamethylenedicarboxylate.
*I*. Thapsate.

*a*. $\delta(CH_2)$ Bending vibrations.
*b*. $\delta_a(CH_2O)$ Vibrations.
*c*. $\delta_s(CH_2O)$ Vibrations.
*d*. $\delta(CH_2{\cdot}CO)$ Vibrations.
*e*. $\delta(CH_2)$ Wagging vibrations.
*f*. $\nu C{-}O$ and $\nu C{-}O{-}C$ Vibrations.
*g*. $\delta(CH_2)$ Rocking vibrations.
*h*. $\delta(CH_2)$ Rocking vibrations or $CO_2CH_2$ vibrations.
*i*. $\delta(CH_2)$ Rocking vibrations.

FIG. 7. *Diethyl esters.*

*A*. Succinate.
*B*. Glutarate.
*C*. Adipate.
*D*. Pimelate { *D*1, tttt confign. / *D*2, tttg confign.
*E*. Suberate.
*F*. Azeläate.
*G*. Sebacate.
*H*. Decamethylenedicarboxylate.
*I*. Thapsate.

*a*. $\delta(CH_2)$ Bending vibrations.
*b*. $\delta_a(CH_2)$ Vibrations.
*c*. $\delta(CH_2CO)$ Vibrations.
*d*. $\delta_s(CH_2)$ Vibrations.
*e*. $\delta(CH_2)$ Wagging vibrations.
*f*. $\nu C{-}O$ and $\nu C{-}O{-}C$ Vibrations.
*g*. Ethyl vibrations.
*h*. $\delta(CH_2)$ Rocking vibrations.

C=O *Stretching Vibrations* (1800—1700 cm.$^{-1}$).—Small frequency shifts of the C=O stretching absorptions occur on going from the liquid to the crystalline state. These are listed in Table 1; malonic and oxalic diesters are also included (for liquid only), and show a splitting of the carbonyl absorptions. However, for $n \geqslant 2$ both the diacids and diesters show single carbonyl bands, indicating only weak coupling across two or more carbon atoms. This is in contrast with the strong coupling across oxygen which results in a split of *ca.* 25 cm.$^{-1}$ for diacyl peroxides [13] and *ca.* 60 cm.$^{-1}$ for acid anhydrides [14] (cf. 30 cm.$^{-1}$ for malonic acid [25]).

There are no consistent differences in $\nu$(C=O) between the crystalline and liquid states, unlike the di- and mono-carboxylic acids in which $\nu$(C=O) was greater in the liquid owing

[13] Davison, *J.*, 1951, 2456.
[14] Randall, Fowler, Fuson, and Dangl, "Infra-red Determination of Organic Structures," Van Nostrand, New York, 1949, 20.

to a reduction in hydrogen bonding. In the dimethyl esters, however, the even members (except $n = 2$) in both crystalline and liquid states have C=O frequencies which are higher than those in the odd members. This is similar to the even–odd alternation discussed by Sinclair *et al.*[15] for monocarboxylic acids with chains longer than $[CH_2]_{11}$ in which the acids with an even $H{\cdot}[CH_2]_n$ chain have maxima at 1705 cm.$^{-1}$ and the acids with an odd $H{\cdot}[CH_2]_n$ chain have maxima at 1698—1701 cm.$^{-1}$.

TABLE 1. *Frequency of carbonyl absorptions,* ν(C:O) (cm.$^{-1}$).

| | | Dimethyl esters | | | Diethyl esters | | |
|---|---|---|---|---|---|---|---|
| *n* | | cryst. | liquid | δν | cryst. | liquid | δν |
| 0 | Oxalate | — | — | — | — | 1754, 1774 | — |
| 1 | Malonate | — | 1750, 1768 | — | — | 1750, 1764 | — |
| 2 | Succinate | 1742 | 1751 | +9 | 1743 | 1753 | +10 |
| 3 | Glutarate | 1740 | 1749 | +9 | 1730 | 1741 | +11 |
| 4 | Adipate | 1754 | 1752 | −2 | 1738 | 1749 | +11 |
| 5 | Pimelate * | I II 1740 (1741) | 1749 | +9 | I II 1738 (1744) | 1739 | + 1 |
| 6 | Suberate | 1751 | 1749 | −2 | 1743 | 1741 | − 2 |
| 7 | Azeläate | 1745 | 1743 | −2 | 1750 | 1745 | − 5 |
| 8 | Sebacate | 1750 | 1755 | +5 | 1740 | 1747 | + 7 |
| 10 | Decamethylenedicarboxylate | 1753 | 1753 | 0 | 1745 | 1733 | −12 |
| 14 | Thapsate | 1750 | 1755 | +5 | 1750 | 1743 | − 7 |
| | Even ($n \geqslant 4$) = | 1750—1754 | 1749—1755 | — | 1738—1750 | 1733—1753 | — |
| | Odd ($n \geqslant 3$) = | 1740—1745 | 1743—1749 | — | 1730—1750 | 1739—1745 | — |

* I = tttt Configuration, II = tttg configuration; see p. 932.

C–H *Bending Vibrations* (1500—1300 cm.$^{-1}$).—In the dicarboxylic acids,[2] there are three distinct bands in the 1500—1400 cm.$^{-1}$ region at 1475, 1435, and 1415 cm.$^{-1}$ which are assigned respectively to a normal $CH_2$ bending vibration, a dimeric carboxyl vibration, and a $CH_2$ bending mode, adjacent to a C=O group. In the diesters we expect the bands at *ca.* 1475 and *ca.* 1415 cm.$^{-1}$ to persist, together with absorptions arising from the methyl and ethyl groups.

The dimethyl esters all show a medium absorption at 1435—1445 cm.$^{-1}$ in both crystalline and amorphous phases, which is assigned [16] to the symmetrical bending mode of a methyl group attached to an oxygen atom, $\delta_s(CH_3O)$. The weaker $\delta_s(CH_3O)$ at *ca.* 1460 cm.$^{-1}$ is not resolved in most cases owing to overlapping $\delta(CH_2)$ bending and $\delta_s(CH_3O)$ vibrations. However, a shoulder at *ca.* 1462 cm.$^{-1}$ in the spectrum of dimethyl succinate is probably due to this mode.

The diethyl esters show a more complex series of bands in this region. Absorptions at *ca.* 1480 and *ca.* 1420 cm.$^{-1}$ are assigned respectively to a normal $CH_2$ bending vibration and a bending mode of $CH_2$ adjacent to a carbonyl group as for the dimethyl esters. The band at *ca.* 1480 cm.$^{-1}$ is split in the longer-chain diethyl esters. This is attributed to $CH_2$ groups in two different environments, in the terminal ethyl groups and in the polymethylene chain. Bands at *ca.* 1380 cm.$^{-1}$ ($n = 5$—14) are attributed to $\delta_s(CH_3)$ and a variable series of absorptions at *ca.* 1450 cm.$^{-1}$ is assigned to $\delta_a(CH_3)$. These two sets of absorptions are common to all paraffin-type compounds.[5] In the shorter-chain esters ($n = 2$—4), the $\delta_s(CH_3)$ is shifted from 1380 cm.$^{-1}$ and appears [17,18] at *ca.* 1395 cm.$^{-1}$ owing probably to interaction with wagging vibrations of the polymethylene chain. Two series of $CH_2$ wagging vibrations can be traced in the diethyl esters with origins at 1378 and 1321 cm.$^{-1}$ in diethyl succinate (cf. alkyl bromides [8] and monocarboxylic acids [3]). Bands at 1376 and 1337 cm.$^{-1}$ in the spectrum of liquid diethyl malonate may also form part of this distribution.

Two similar series of $CH_2$ wagging vibrations can be traced in the spectra of the dimethyl

[15] Sinclair, McKay, and Jones, *J. Amer. Chem. Soc.*, 1952, **74**, 2570.
[16] Sheppard, *Trans. Faraday Soc.*, 1955, **51**, 1465.
[17] Nolin and Jones, *Canad. J. Chem.*, 1956, **34**, 1382.
[18] *Idem, ibid.*, p. 1392.

esters with origins at 1315 cm.$^{-1}$ in the spectrum of dimethyl succinate and 1395 cm.$^{-1}$ in that of dimethyl glutarate.

The frequencies of bands in these series are listed in Table 2. The assignments in this Table are strengthened by the fact that, for the most part, corresponding bands appear in the spectra of the dicarboxylic acids (see crosses in Figs. 1—5). In the longer-chain diesters, more especially the dimethyl esters, the lower-frequency series overlaps the ν(C–O) vibrations.

TABLE 2. $\delta CH_2$ *Wagging frequencies* (*crystalline state*) (cm.$^{-1}$).

| | Dimethyl | Diethyl | Dimethyl | Diethyl |
|---|---|---|---|---|
| $n = 1$ | — | 1376 * | 1346 * | 1337 * |
| $n = 2$ | — | 1378 | 1315 | mean = 1321 (1327, 1315) |
| $n = 3$ | 1395 | —† | mean = 1293 (1304 sh, 1282) | —† |
| $n = 4$ | 1390 | 1367 | 1262 | 1260 |
| $n = 5$ | I mean = 1374 (1385, 1363) | I 1359 | I mean = 1252 (1258, 1247 sh) | I 1249 |
| $n = 6$ | 1340 | 1330 | 1246 | 1240 |
| $n = 7$ | 1315 | 1319 | 1233 | 1235 |
| $n = 8$ | 1290 | mean = 1300 (1305, 1294) | 1220 ‡ | 1222 |
| $n = 10$ | 1275 | 1275 | 1215 ‡ | 1220 |
| $n = 14$ | 1249 | 1250 | 1205 ‡ | 1205 |

* Liquid.
† Not *trans*.
I = tttt Configuration (see below).
‡ Overlap C–O vibrations.

*Absorptions below* 1300 *cm.*$^{-1}$.—Bands at *ca.* 1170—1180 and *ca.* 1200 cm.$^{-1}$ in the spectra of the dimethyl esters and at *ca.* 1180—1190 and 1165—1170 cm.$^{-1}$ in those of the diethyl esters are assigned to ν(C–O) and ν(C–O–C) vibrations.[15,20] In the longer-chain diesters ($n$ = 8—14), these absorptions overlap the $\delta CH_2$ wagging distribution, resulting in slightly anomalous frequencies.

Comparison of the crystalline-state spectra of the diesters with those of the corresponding dicarboxylic acids supports the assignment of bands at *ca.* 950 and 1030 cm.$^{-1}$ in the spectra of the diethyl esters to absorptions characteristic of ethyl groups. The dimethyl esters have absorptions at 880 and 990 cm.$^{-1}$ which are attributed to methyl absorptions, the latter to a methyl rocking mode [17,19] and the former possibly to a methoxycarbonyl vibration.[17,19] These assignments are confirmed by a comparison of the spectra of some simple esters, *viz.*, methyl and ethyl formate, methyl and ethyl acetate, methyl and ethyl benzoate, etc.[20]

$\delta[CH_2]_n$ *Rocking Vibrations.*—In the crystalline-state spectra of both the dimethyl and the diethyl esters, three series of absorptions in the 900—700 cm.$^{-1}$ region can be traced which are very similar to those observed in the di- and mono-carboxylic acids of corresponding chain lengths. These are assigned to $\delta[CH_2]_n$ rocking modes of the *trans*-zigzag chain. Diethyl glutarate is an exception, and this is taken as evidence for this ester's having a non-*trans*-configuration in the crystalline state.

Crystalline dimethyl and diethyl pimelate exhibit two different spectra depending upon the conditions of crystallisation. These differences may be due to two polymorphic modifications of which those with the lower $\delta[CH_2]_n$ frequency, *i.e.*, 731 cm.$^{-1}$ for the dimethyl ester and 728 cm.$^{-1}$ for the diethyl ester, are taken as having the planar *trans*-configuration. The higher frequencies, *i.e.*, 734 and 737 cm.$^{-1}$ for the dimethyl and the diethyl esters respectively, probably correspond to a slightly twisted planar tttt configuration or to a tttg isomer (t = *trans*, g = *gauche* [11]); any other isomer would have its main rocking mode at a higher frequency than that observed. A similar metastable polymorph was reported for glutaric acid.[3]

[19] Günthard, *Helv. Chim. Acta*, 1953, **36**, 1149.
[20] Thompson and Torkington, *J.*, 1945, 640.

The lowest series of $[CH_2]_n$ rocking absorptions for the diesters are listed in Table 3, together with those for the corresponding dicarboxylic acids,[2] polyesters,[1] and hydrocarbons.[5,6]

TABLE 3. $\delta[CH_2]_n$ *Rocking frequencies for* $X\cdot[CH_2]_n\cdot X$ *type molecules.*

(cm.$^{-1}$)

| | | | $X = CO_2Me$ | | $X = CO_2Et$ | | |
|---|---|---|---|---|---|---|---|
| $n$ | $X = H$ | $X = CO_2H$ | Cryst. | Liquid | Cryst. | Liquid | Polyesters |
| 2 | 822 | 804 | 797 sh, 778 | 805 | 819 sh, 800, 777 sh | 804 | 800—810 |
| 3 | 748 | 754 | 760, 720 | 751 | 815 † | 754 | — |
| 4 | 732 | 733 | 735 | 750 | 735 | 733 | 733—740 |
| 5 | 728 | 731 | 731 (734 *) | 741 | 728 (737 *) | 731 | — |
| 6 | 726 | 725 | 728 | 732 | 730 | 725 | — |
| 7 | 723 | 726 | 724 | 726 | 723 | 726 | — |
| 8 | 722 | 722 | 730 | 724 | 724 | 722 | 720—725 |
| 9 | 721 | — | — | — | — | — | — |
| 10 | 720 | 723 | 720 | 722 | 723 | 723 | — |
| 11 | 720 | — | — | — | — | — | — |
| 12 | 722 | — | — | — | — | — | — |
| 13 | 723 | — | — | — | — | — | — |
| 14 | 722 | 727, 721 | 731, 720 | 720 | 730, 720 | 721 | — |
| 15 | — | — | — | — | — | — | — |
| 16 | — | 727, 720 | — | — | — | — | — |

* Slightly twisted *trans*-chain or tttg. † Non-*trans*-configuration, probably tg.

TABLE 4. *Physical constants of esters.*

| | Literature | | Observed | |
|---|---|---|---|---|
| | B. p./mm. | M. p. | B. p./mm. | M. p. |
| Dimethyl succinate | 195·2°/760 | 19° | 200°/760 | — |
| | | | 145°/150 | |
| Diethyl ,, | 217·7°/760 | −21° | 212°/760 | — |
| Dimethyl glutarate | 222°/760 | — | 217°/760 | — |
| | 84·5°/6 | | 105°/20 | |
| Diethyl ,, | 240°/760 | −24·1° | 230°/760 | — |
| | 103—104°/7 | | 115°/20 | |
| Dimethyl adipate | 242°/760 | 8° | 235°/760 | — |
| | 112°/10 | 0° * | 120°/20 | |
| Diethyl ,, | 245°/760 | — | 238°/760 | — |
| Dimethyl pimelate | 257°/760 | — | 255°/760 | — |
| | 130—135°/17 | | 139°/23 | |
| Diethyl ,, | 252—255°/748 | — | 282°/760 | — |
| | | | 152°/15 | |
| Dimethyl suberate | 268°/760 | −3·1° | 270°/760 | — |
| | 174—175°/13—20 | | 146—149°/20 | |
| Diethyl ,, | 282°/763 | 5·9° | 284°/760 | — |
| | | | 160—163°/20 | |
| Dimethyl azelaate | 281°/760 | — | 281°/760 | — |
| | 140—141°/9 | | 158—162°/22 | |
| Diethyl ,, | 291°/760 | — | 291°/760 | — |
| | 148°/7·5 | | 155—165°/16 | |
| Dimethyl sebacate | 293°/754 | 26·4° | 288°/763 | — |
| | 175°/20 | (38°) | | |
| Diethyl ,, | 306°/773 | 1·25° | 312°/760 | — |
| | 158—159°/7·5 | — | 179—181°/17 | |
| Dimethyl decamethylenedicarboxylate | 167—169°/9 | 31° | — | 26·7° |
| Diethyl ,, ,, | 347°/760 | — | 339°/760 | — |
| | 204—205°/5 | *ca.* 16° | 210—212°/25 | |
| Dimethyl thapsate | — | 51—52° | — | 40° |
| Diethyl ,, | — | 39° | — | 30° |

* Freezing point.

In the liquid-state spectra, however, the *trans*-$\delta[CH_2]_n$ rocking absorptions are still present, although weaker. In the longer-chain esters, only one band at *ca.* 722 cm.$^{-1}$ is present in the liquid-state instead of at least two in the crystalline-state spectra. As the splitting of the 722 cm.$^{-1}$ band in long-chain compounds is attributed to coupling of $\delta[CH_2]_n$

rocking vibrations between adjacent molecules in the orthorhombic unit cell,[21,22] the diesters may crystallise with this symmetry also. In particular, the crystalline diesters cannot have the hexagonal packing suggested for the fatty acids just below their melting points,[3,21,23] nor a triclinic unit cell.[24]

In the liquid-state spectra of the shorter-chain esters, several bands appear in the 1000—700 cm.$^{-1}$ region which are not present in the crystalline-state spectra. These are thought to arise from the presence of discrete rotational isomers in the liquid state, *e.g.*, dimethyl and diethyl glutarate can exist as tt, gt, and gg types.[11] As the chain is increased in length, the number of possible rotational isomers increases markedly, and in the longer-chain esters, a dynamic mixture of a large number of rotational isomers would give a spectrum which was indistinguishable from the product of non-discrete rotational isomerism.

We thank Dr. G. B. Barlow for preparing several of the diesters, and the Dunlop Rubber Company for permission to publish this work.

Chemical Research Department,
Dunlop Research Centre, Birmingham, 24.
[Present address (W. H. T. D.): Tube Investments Research Laboratories,
Hinxton Hall, Cambridge.] [*Received, July 22nd*, 1957.]

[21] (*a*) Stein and Sutherland, *J. Chem. Phys.*, 1954, **22**, 1993; (*b*) Stein, *ibid.*, 1955, **23**, 734.
[23] Chapman, *Nature*, 1955, **176**, 216.
[23] Malkin, "Progress in the Chemistry of Fats and Other Lipids," Pergamon Press Ltd., London, 1952, **1**, 8.
[24] Chapman, Colloquium Spectroscopicum Internationale VI, Amsterdam, May, 1956.
[25] Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen, London, 1954, 145.

---

## 188. *The Application of Infrared Spectroscopy to a Study of Some Reaction Intermediates and Products of the Autoxidation of Long-chain Olefins.**

By (Mrs.) J. Gold.

The action of gaseous oxygen on methyl oleate and elaidate, long-chain α-diols, epoxides, α-ketols, and α-diketones has been examined. No "elaidinisation" of methyl oleate occurs during autoxidation, suggesting that *trans*-hydroperoxides are formed from both methyl oleate and elaidate. α-Diols and *cis*- and *trans*-epoxides are not oxidised, but α-ketols and α-diketones are, forming smaller acids by way of hydroperoxides, α-diketones being intermediates in the oxidation of α-ketols. α-Diols and α-ketols are poly-esterified in the presence of free carboxylic acid. The configurations of the epoxide (*cis* and *trans*) and α-diol (*threo* and *erythro*) products of olefin autoxidation are related to the geometrical isomerism of the initial olefin. A general scheme of olefin autoxidation is outlined.

In recent years the autoxidation products of several olefinic compounds have been isolated. These consist mainly of α-diols, epoxides, scission acids, and minor amounts of α-ketols.[1] Less attention has been paid to the mode of formation of these products from olefins, their interaction, their behaviour on further oxidation to ascertain whether they are intermediates or end-products, and their configuration in relation to that of the olefinic starting material. Some of these problems have now been attacked and the results allow a statement of the broad features of a general reaction scheme for the complex autoxidation of olefins. The compounds specifically investigated were methyl oleate and elaidate; α-ketols, α-diketones, *cis*- and *trans*-epoxides, and *threo*- and *erythro*-diols derived

* For a preliminary account, see *Research*, 1956, **9**, 519.

[1] (*a*) Skellon, *J. Soc. Chem. Ind.*, 1931, **50**, 382T; (*b*) Ellis, *Biochem. J.*, 1950, **46**, 129; (*c*) Feuell and Skellon, *J.*, 1954, 3414.

from octadecenoic acids; as well as lauroin and the corresponding diketone, tetracontane-12 : 13-dione.

## Experimental

Autoxidations were carried out in the presence of uranium petroselinate (0·2% by wt.) at 120°, unless stated otherwise. Samples were withdrawn and analysed chemically [2] and spectroscopically. The infrared spectra of liquids were determined as films, and those of solids as Nujol mulls.

*Autoxidation of Methyl Oleate* (*Octadec*-cis-9-*enoate*) *and Elaidate* (*Octadec*-trans-9-*enoate*).—*Infrared spectroscopic analysis.* Infrared absorption spectra were taken on a Grubb-Parsons double-beam instrument on thin films of the oils by themselves, in a cell with adjustable path-length. For short path-lengths an internal standard, *viz.*, the band at 3·46 μ (for methyl elaidate) or 3·48 μ (for methyl oleate), which is due to C–H stretching vibrations, was used, the concentration $c$ of any particular group present during the oxidation being given by $c$ = Constant × $D_a/D_b$, where $D_a$ = optical density at which the group absorbs, and $D_b$ = optical density at the wavelength of the " standard " band. This relation was used in the analysis of unsaturation and of carboxyl and hydroxyl groups. For thicker films the use of an internal standard was unnecessary. Where checked, both methods gave identical results, except at the highest absorption intensities.

*Autoxidation of esters.* Methyl oleate (b. p. 168—170°/2 mm.; from oleic acid purified by low-temperature crystallisation from acetone) or methyl elaidate (b. p. 199—200°/8·5 mm.) was oxidised in a wide tube with a deep ground-glass joint, the stopper of which was equipped with an inlet delivery tube tapered to a fine nozzle, outlet, stirrer guide, and apertures for a thermometer and for removal of samples. Oxygen, dried by concentrated sulphuric acid, was admitted at a rate of 50 ml. per min., and stirring was at approx. 200 r.p.m. The results are in Tables 1 and 2, to which the following notes apply.

(*a*) Obtained from 100 × ratio of [Constant × $D_{10\cdot32}/D_{3\cdot46}$ (for methyl elaidate)] to the theoretical initial oidine value, where the constant = 85·61 ÷ $D_{10\cdot32}/D_{3\cdot46}$ (initial).

(*b*) Given by 100 × ($D_{3\cdot18}/D_{3\cdot48}$) less initial value.

(*c*) Calculated from the actual acid value and the theoretical maximum acid value (on the assumption that all the methyl elaidate is quantitatively converted into scission acids, $CH_3{\cdot}[CH_2]_n{\cdot}CO_2H$ and $CO_2H{\cdot}[CH_2]_{13-n}{\cdot}CO_2Me$ and $CO_2$).

(*d*) Given by 100 ($D_{6\cdot1}/D_{3\cdot46}$) less the initial value. After 390 min. accurate measurement was impossible, because of the general increase in intensity at 5—6 μ.

(*e*) Calculated from the actual active-O % and oxiran-O % and the theoretical values (4·87, 5·119) for the hydroperoxide and epoxide, respectively.

(*f*) *I.e.*, sap. val. − (acid val. + initial sap. val.).

Table 1. *Autoxidation of methyl elaidate* (25 *g.*).*

| Time (min.) | 0 | 12 | 35 | 72 | 130 | 210 | 285 | 290 | 390 | 450 | 515 | 575 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Unsaturation (%) | | | | | | | | | | | | |
| Spectroscopic[a] | 100 | — | 98 | 98 | 86 | 57 | 31 | — | 15 | 7 | 5 | 4 |
| Chemical | 100 | 99 | 100 | 97 | — | 67 | 46 | — | 27 | 17 | 11 | 8 |
| Intensity of band at 3·18 μ[b] | 0·0 | — | 0·4 | 0·6 | 1·0 | 4·0 | 8·0 | — | 12·3 | 15·1 | 17·5 | 19·3 |
| Carboxyl (%) (chemical)[c] | 0·0 | — | — | — | 1·5 | 5·8 | — | — | 18·0 | 20·5 | — | 25·1 |
| Intensity of band at 6·1 μ[d] | 0·0 | — | 0·0 | 0·0 | 1·7 | 4·9 | 7·0 | — | 6·4 | — | — | — |
| Hydroperoxide (%)[e] | 0·0 | — | — | 5·3 | 16·3 | 17·8 | 11·4 | — | 6·3 | 5·2 | — | 4·2 |
| Epoxide (%)[e] | 0·0 | — | — | — | 5·7 | — | — | 11·0 | — | 9·4 | — | 5·3 |
| α-Diol (%) | 0·0 | — | — | 0·0 | — | 6·1 | — | — | 10·6 | — | — | 12·0 |
| Sap. val. | 189 | — | — | 190 | — | — | 236 | — | — | 286 | 315 | 336 |
| Additional ester[f] | 0 | — | — | 1 | — | — | 11 | — | — | 31 | 52 | 66 |

* For notes see main text.

*Spectroscopic analysis of carbonyl groups.* Both methyl elaidate and oleate show [3] single carbonyl bands at 5·75 μ. In both cases bands, at 5·81, 5·85, 6·1, and later at 5·6 μ appeared

[2] Analyses: peroxide, Skellon and Wills, *Analyst*, 1948, **73**, 78; epoxide, Swern, Findley, Billen, and Scanlan, *Analyt. Chem.*, 1947, **19**, 414; hydroxyl, Ogg, Porter, and Willits, *Ind. Eng. Chem. Anal.* 1945, **17**, 394; other analyses, Knight and Swern, *J. Amer. Oil Chemists' Soc.*, 1949, **26**, 366.

[3] Shreve, Heether, Knight, and Swern, *Analyt. Chem.*, 1950, **22**, 1498.

XUM

TABLE 2. *Autoxidation of methyl oleate* (25 g.).*

| Time (min.) | 0 | 50 | 60 | 100 | 125 | 187 | 220 | 340 | 460 | 490 | 570 | 580 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Unsaturation (%) | | | | | | | | | | | | |
| Chemical | 100 | — | — | 75 | 67 | — | 43 | 27 | 20 | — | — | — |
| Intensity of band at 3·18 μ [a] | 0·0 | 0·0 | — | — | 2·5 | 4·5 | — | 8·5 | — | 11·7 | 13·3 | — |
| Carboxyl (%) [a] | 0·0 | — | — | — | 2·7 | 4·3 | — | 9·5 | — | 15·0 | 18·7 | — |
| Hydroperoxide (%) [a] | 0·0 | — | 11·7 | 21·4 | — | — | 19·3 | 12·7 | 6·4 | — | — | 4·1 |
| Epoxide (%) [a] | 0·0 | — | — | — | 6·5 | — | — | 11·3 | — | — | — | 5·1 |
| α-Diol (%) | 0·0 | 0·0 | — | — | — | — | 6·0 | — | — | — | — | 10·5 |
| Sap. val. | 189 | — | — | — | 210 | — | 229 | — | — | 318 | 351 | — |
| Additional ester [f] | 0 | — | — | — | 12 | — | 22 | — | — | 80 | 102 | — |

* For notes see main text.

and increased in intensity as the oxidation proceeded. The following products were separated from the autoxidation residue from methyl elaidate (oxidised for 575 min. at 120°): (1) Free acidic products separated by alkaline extraction followed by acidification [bands at 5·70 (sh = shoulder), 5·75(sh), 5·80, 5·85, 5·91 μ]. (2) Neutral products remaining after products (1) had been removed [bands at 5·6 (broad sh), 5·75, 5·81, 5·84(sh), 6·1(sh) μ]. These neutral products were hydrolysed, and the acids (3) separated [bands at 5·76, 5·80, 5·86, 5·92 μ similar to those of (1)]. After removal of the acids (3) from material (2), the product gave bands at 5·6(small sh) and 5·75 μ. Therefore the bands at 5·81 and 5·85 μ must be due, at least in part, to acidic products.

Autoxidised methyl elaidate (at 120°) shows a band at 6·1 μ [also apparent in material (2), above]. This could be due to *cis*-ethylenic compounds [4] or αβ-unsaturated ketones.[5] The band is assigned to the latter, since the band is more intense than that in *pure* methyl oleate and occurs at a longer wavelength. Also, the intensity of the band is greater in methyl elaidate autoxidised for 20 hr. at 85° [hydroperoxide 28·5%: unsaturation (iodometric) 42% and (spectroscopic) 38%] and αβ-unsaturated ketones are known to be formed in greater amount at this lower temperature.[1b] The band at 5·6 μ may possibly be due to saturated lactones, since it is almost completely removed by hydrolysis.

*Autoxidation of α-Ketols.*—Autoxidation of 6 : 7- and 7 : 6-hydroxyoxostearic acids led to oils of high molecular weight, as a result of some polyesterification, and separation of the products appeared unpromising from preliminary experiments.

*Autoxidation of lauroin.* Lauroin (3·8 g.), m. p. 61° (prepared by Hansley's method [6]), was oxidised for 8·5 hr. Volatile products were collected at −78°. Carbon dioxide evolved was estimated by reaction with barium hydroxide. Carbonyl analysis fell continuously and a maximum peroxide value of 0·03 (active O%) was obtained after 165 min.

The residue (2 g.; acid value, 150) after the oxidation was dissolved in ether and treated with sodium carbonate solution, and the two layers were separated.

The neutral ethereal extracts were washed with aqueous sodium carbonate, then water, and dried ($Na_2SO_4$). After removal of the ether, the cooled residue gave, on fractional crystallisation from ethanol, pale yellow crystals (0·2 g.), m. p. 70° (mixed m. p. with tetracontane-12 : 13-dione, 71°) and a more soluble cream-coloured solid (0·4 g.), m. p. 58° (mixed m. p. with lauroin, 61°). The alkaline aqueous layer was acidified and extracted with ether. The extracts were dried ($Na_2SO_4$), the ether was evaporated, and the residue (1·1 g.) crystallised from ethanol to m. p. 37°. The m. p. of the *p*-bromophenacyl derivative was 72° alone or mixed with that of dodecanoic acid, but was depressed to 64—65° on admixture with that of undecanoic acid (m. p. 68°). The condensed volatile matter consisted of traces of water and an immiscible colourless liquid (0·1 g.). This gave a pink colour with Schiff's reagent, indicating the presence of an aldehyde, and an infrared spectrum identical with that of lauric acid, presumably formed by oxidation of the aldehyde. The 2 : 4-dinitrophenylhydrazone (m. p. 103°) gave no m. p. depression on admixture of that of undecanal (m. p. 104°).

6 : 7-*Dioxostearic Acid.*—The mixed 6 : 7- and 7 : 6-hydroxyoxostearic acids (5 g.) were added to chromic acid (3 g.) in glacial acetic acid (300 ml.) with shaking. After 36 hr. at room temperature the solution was diluted with water (300 ml.). The solid precipitate was filtered off and recrystallised from ethanol as pale yellow crystals, m. p. 97° (2·3 g., 46%) (Found: C, 69·0;

[4] McCutcheon, Crawford, and Welsh, *Oil and Soap*, 1941, **18**, 9.
[5] Sinclair, McKay, Myers, and Jones, *J. Amer. Chem. Soc.*, 1952, **74**, 2578.
[6] Hansley, *J. Amer. Chem. Soc.*, 1935, **57**, 2303.

H, 10·1. Calc. for $C_{18}H_{32}O_4$: C, 69·2; H, 10·3%). Steger and van Loon [7] report m. p. 98° for 6 : 7-dioxostearic acid, prepared by potassium permanganate oxidation of octadec-6-ynoic acid.

*Methyl* 9 : 10-*Dioxostearate.*—Methyl *threo*-9 : 10-dihydroxystearate (5 g.) was oxidised by the same method to give, on recrystallisation from ethanol, pale yellow *methyl* 9 : 10-*dioxostearate*, m. p. 50° (2·9 g., 58%) (Found: C, 69·8; H, 10·3. $C_{19}H_{34}O_4$ requires C, 69·9; H, 10·5%).

*Methyl* 6 : 7-*Dioxostearate.*—Methyl *threo*-6 : 7-dihydroxystearate (1 g.) was oxidised as above to give, on recrystallisation from ethanol, pale yellow *methyl* 6 : 7-*dioxostearate*, m. p. 61° (0·5 g., 51%) (Found: C, 69·75; H, 10·3%).

*Tetracontane*-12 : 13-*dione.*—This diketone, m. p. 71° (5 g., 50%), was prepared as above from lauroin (10 g.). Hansley [8] reports m. p. 71·0—71·5° for the same compound, prepared by oxidation of lauroin with Wijs's solution.

*Autoxidation of* α-*Diketones.*—6 : 7-*Dioxostearic acid.* After 475 minutes' oxidation the infrared spectrum (liquid film) is similar to, and contains all, the absorption bands of adipic acid and additional bands at 8·07, 7·77, and 9·24 μ. These are present in the spectrum of lauric acid. After 475 min. the acid value (initial 177) and saponification value were 305 and 418 respectively.

*Autoxidation of tetracontane*-12 : 13-*dione.* The results were:

| Time of oxidation (min.) | 0 | 100 | 240 | 300 | 525 | 575 |
|---|---|---|---|---|---|---|
| Peroxide [active O (%)] | 0·00 | 0·30 | 0·27 | 0·14 | 0·00 | — |
| Carbonyl (%) | 15·3 * | — | — | 9·0 | — | — |
| Unsaturation (I value) | — | 5·1 | 6·0 | — | — | — |
| $CO_2$ (g.) (from 5·3 g. of diketone) | — | — | — | — | — | 0·13 |

* Theor. initial value, 15·3.

The residue (2·0 g.; acid value, 157) from the oxidation of 5·3 g. of diketone for 575 min. was dissolved in ether and extracted with sodium carbonate solution. The alkaline layer was separated and acidified, the liberated acids were extracted with ether, and the extracts dried ($Na_2SO_4$). After evaporation of the ether, the residue was cooled and recrystallised from ethanol to m. p. 39° (1·2 g.). The compound was identical (mixed m. p. and infrared spectrum) with lauric acid. Its *p*-bromophenacyl derivative had m. p. 72° alone or mixed with that of lauric acid.

The neutral ethereal extract was dried ($Na_2SO_4$) and the ether evaporated. The semi-solid residue (two of its infrared absorption bands were at 2·90 and 6·11 μ) gave some tetracontane-12 : 13-dione (0·05 g.; identified by mixed m. p.) on attempted crystallisation from ethanol. Evaporation of the ethanolic mother-liquor gave a semisolid residue (0·3 g.) which was not identified. The volatile matter collected in the trap consisted of traces of water and an aldehyde (0·3 g.) identified as previously as undecanal.

*Autoxidation of methyl* 9 : 10-*dioxostearate.* The results were:

| Time of oxidation (min.) | 0 | 50 | 110 | 205 | 345 |
|---|---|---|---|---|---|
| Peroxide [active O (%)] | 0·00 | 0·00 | 0·15 | 0·05 | 0·00 |
| $CO_2$ (g.) (from 3 g.) | — | — | — | — | 0·11 |

The residue (1·2 g.), from the oxidation of methyl 9 : 10-dioxostearate (3 g.) for 6 hr., was dissolved in ether and extracted with aqueous sodium carbonate. The alkaline extract was acidified and steam-distilled. Solid zinc sulphate was added to the neutralised distillate, and the solid precipitate was filtered off, recrystallised from ethanol, and identified as zinc nonoate (m. p. 133° alone or mixed with zinc nonoate). The cooled residue from the distillation was hydrolysed, acidified, and extracted with ether. These extracts were dried ($Na_2SO_4$) and the solvent evaporated. The residual azelaic acid, on crystallisation from water, had m. p. 107° (mixed m. p. and infrared spectrum).

The neutral ethereal extract was dried, and the solvent evaporated. A liquid film of the cooled residue gave a spectrum including, amongst others, bands at 2·90 and 6·11 μ. No methyl 9 : 10-dioxostearate was recovered. A spectrum of the condensed volatile matter gave absorption maxima corresponding to those of a mixture of azelaic acid and water.

*Effect of Heat and Gaseous Oxygen on Epoxides and Diols.*—*Methyl* trans-9 : 10-*epoxystearate.* When the ester (m. p. 32°; 5·5 g., prepared from methyl elaidate by oxidation with perbenzoic acid [8]) was treated with gaseous oxygen, analyses for oxiran-oxygen and peroxide indicated

[7] Steger and van Loon, *Rec. Trav. chim.*, 1933, **52**, 593.
[8] Swern, "Organic Reactions," John Wiley and Sons, New York, 1953, Vol. VII, p. 396.

XUM

that no oxidation had occurred. The spectra were all identical with the spectrum of the pure *trans*-epoxide (identical with that published [9] for the same compound).

The infrared spectrum was unchanged when the *trans*-epoxide (0·5 g.) was heated in a sealed tube at 120° for 7 hr.

*Methyl* cis-6 : 7-*epoxystearate*. The above experiment was repeated with methyl *cis*-6 : 7-epoxystearate, m. p. 27° (prepared from methyl petroselinate by oxidation with perbenzoic acid). The infrared spectra of the *cis*-epoxide before and after attempted oxidation for 7 hr., and after 7 hours' heating alone were identical. The spectra of the *cis*- and *trans*-epoxides were determined in all cases as liquid films. The epoxides in the solid or partially crystalline state give more detailed spectra and have bands at slightly different wavelengths.

erythro-6 : 7-*Dihydroxystearic acid* (m. p. 121°; 18 g.). The molten acid (prepared from petroselinic acid by oxidation with alkaline potassium permanganate) was oxidised for 540 min. at 123°:

| | | | | | |
|---|---|---|---|---|---|
| Time (min.) | 0 | 150 | 270 | 420 | 540 |
| Carboxyl (%) | 93·1 | 77·3 | 74·4 | 70·9 | 69·7 |
| Hydroxyl (%) | — | 83·6 | 73·0 | 59·1 | 49·0 |

The pale yellow product (2·0 g.; m. p. 92—93°; mean *M*, 450; initial *M*, 317; sap. val., 273; ester val., 149; carbonyl %, 0·0; oxiran-O %, 0·0) was hydrolysed, then treated with chloroform–light petroleum to extract any hydroxyoxo-acids present. Only unchanged *erythro*-6 : 7-dihydroxystearic acid (1·3 g.) was recovered, in addition to a trace of oil with a sweet ester odour.

threo-9 : 10-*Dihydroxystearic acid*. The acid (m. p. 95°; 18 g.) (prepared both from oleic and from elaidic acid by oxidation with formic acid and hydrogen peroxide,[8] and aqueous alkaline potassium permanganate, respectively) was oxidised for 500 min.:

| | | | | |
|---|---|---|---|---|
| Time (min.) | 0 | 130 | 310 | 440 |
| Carboxyl (%) | 96·8 | 92·5 | 89·7 | 88·7 |
| Hydroxyl (%) | 95 | — | 53 | 43 |

The product had *M*, 440 (initial *M*, 317), m. p. 71·5—73°, oxiran-O %, 0·0.

*Methyl* threo-9 : 10-*dihydroxystearate*. The ester, m. p. 93°, was prepared from methyl oleate, acetic acid, and hydrogen peroxide by adaptation of Dorée and Pepper's method[10] for methyl 13 : 14-dihydroxybehenate. Analyses for hydroxyl, ester, carbonyl, and epoxide groups during treatment with gaseous oxygen for 600 min. indicated absence of oxidation. However, when the above ester was heated with azelaic acid in a closed vessel for 415 min. at 120°, the acid and hydroxyl values fell from 280 and 186 to 248 and 146, respectively. Under the same conditions, no reaction occurred between the ester and methyl *trans*-9 : 10-epoxystearate.

*Isolation of Dihydroxy-acid from Autoxidised Methyl Elaidate*.—A procedure similar to that used by King [11] was employed. The isolated dihydroxystearic acid, m. p. 129—130°, gave an infrared spectrum which was identical with that of pure *erythro*-9 : 10-dihydroxystearic acid.

*Isolation of Dihydroxy-acids from Autoxidised Methyl Oleate*.—The accurately weighed product (*ca.* 2 g.) from the autoxidation of methyl oleate at 120° was hydrolysed, diluted with water, acidified, and cooled. The mixture was then extracted with ether, the ethereal extracts were dried ($Na_2SO_4$), and the solvent was evaporated. Light petroleum (b. p. 40—60°; 100 ml.) was added to the residue, and the mixture stirred and cooled in the refrigerator overnight. The white solid precipitate, m. p. 100—105°, was filtered off through a weighed sintered-glass crucible, washed with light petroleum, dried, and weighed. Its infrared spectrum showed the compound to be a mixture of *erythro*- with some *threo*-9 : 10-dihydroxystearic acid. A spectrum of the same mixture, after recrystallisation from ethanol, showed that the proportion of the *threo*-form had increased.

## Discussion

*Scheme of Olefin Autoxidation*.—A study of the intensity of the band at 10·32 μ (associated with a *trans*-double bond [12]) during the autoxidation of methyl elaidate shows that the double bond is scarcely attacked in the initial stages when the hydroperoxide

[9] Shreve, Heether, Knight, and Swern, *Analyt. Chem.*, 1951, **23**, 277.
[10] Dorée and Pepper, *J.*, 1942, 477.
[11] King, *J.*, 1954, 2114.
[12] Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen and Co., London, 1954.

XUM

concentration [as shown by chemical analysis (Table 1) and the intensity of the band at 2·9 μ [13]] is increasing, and that the most rapid decrease in unsaturation occurs simultaneously with hydroperoxide decomposition and the onset of secondary reactions. These analyses support the view that the formation of an unsaturated hydroperoxide [14] is the initial stage of olefin autoxidation. [In addition the spectroscopic analysis for unsaturation allows a comparison with Wijs's method based on iodine absorption (Table 1). Discrepancies may be due to the unreliability of the latter in the presence of peroxide.[15]] Moreover the fact that 2 : 2 : 5 : 5-tetramethylhex-3-ene and 1 : 2-diphenylethylene (both lacking α-methylenic groups) will not undergo autoxidation in the absence of a hydroperoxide [16] suggests that initiation occurs at the α-methylenic group [14] (cf. ref. 17).

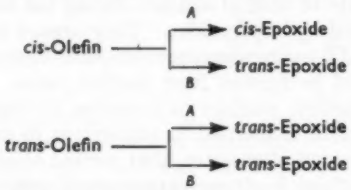
No evidence for the formation of *cis*-olefin during the autoxidation of methyl elaidate was obtained, from examination of either the absorption near 6 μ or the region about 13·8 μ. These observations accord with the fact that no traces either of *cis*-epoxide [18] or of *threo*-9 : 10-dihydroxystearic acid were isolated from the autoxidation products of methyl elaidate. It is therefore concluded that methyl elaidate does not isomerise to methyl oleate during the oxidation. Since the *cis–trans* equilibrium [19] in the elaidinisation of oleic acid is 1 : 2, production of *cis*-isomer would be expected to be in recognisable amount if the two isomers were in equilibrium during the autoxidation. Knight, Eddy, and Swern [20] observed the growth of the band at 10·32 μ during the autoxidation of methyl oleate at 35°, and showed that the concentration of *trans*-material corresponded to approx. 90% of the concentration of hydroperoxide formed. Their five suggestions for the mode of formation of *trans*-unsaturation can be reduced to two main issues: either there is isomerisation of methyl oleate to methyl elaidate during the oxidation, or methyl oleate gives rise to *trans*-unsaturated hydroperoxides. They argued that in the latter case, *two* *trans*-hydroperoxides (methyl 9-hydroperoxyoctadec-*trans*-10-enoate and 10-hydroperoxyoctadec-*trans*-8-enoate) would be formed from methyl oleate. The observation quoted above, *viz.*, the failure of methyl elaidate to isomerise to methyl oleate, suggests that methyl oleate would also not be isomerised to any extent to methyl elaidate. Thus the present work supports the second alternative, that methyl oleate forms *trans*-unsaturated hydroperoxides. However, there is strong experimental evidence [21] that *four* (not only *two* in the case of methyl oleate; cf. ref. 20) hydroperoxides would be formed from either methyl oleate or elaidate. The formation of *four trans*-hydroperoxides can be reasonably explained (cf. ref. 20) on the assumption that the mesomeric radical, formed by abstraction of an α-methylenic hydrogen atom, does not retain configuration about the site of the initial double bond, and that *trans*-configurations about the two partial double bonds in the radical are preferred.

The results in Table 1 shows that the intensity of the band at 6·1 μ (a measure of the concentration of αβ-unsaturated ketones) reaches a maximum after the maximum concentration of hydroperoxide has been passed, *i.e.*, the formation of unsaturated ketones occurs at a later stage and therefore these are not precursors of the hydroperoxides but are formed from them.[22] The concentration of these unsaturated ketones decreases as they are further oxidised.[23] Chemical analyses, during autoxidation of methyl oleate or elaidate, show that after the growth of hydroperoxide and during its decomposition the

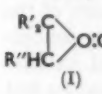
[13] Shreve, Heether, Knight, and Swern, *Analyt. Chem.*, 1951, **23**, 282.
[14] Farmer, *Trans. Faraday Soc.*, 1942, **38**, 340, 356; Farmer and Sutton, *J.*, 1943, 119, 122.
[15] Knight, Coleman, and Swern, *J. Amer. Oil Chemists' Soc.*, 1951, **28**, 498.
[16] Hawkins and Quin, *J. Appl. Chem.*, 1956, **6**, 1.
[17] Hilditch, *J. Oil Colour Chemists' Assoc.*, 1947, **30**, 1.
[18] Ellis, *Biochem. J.*, 1936, **30**, 753.
[19] Griffiths and Hilditch, *J.*, 1932, 2315.
[20] Knight, Eddy, and Swern, *J. Amer. Oil Chemists' Soc.*, 1951, **27**, 188.
[21] Ross, Gebhart, and Gerecht, *J. Amer. Chem. Soc.*, 1949, **71**, 282; Bickford, Fisher, Kyame, and Swift, *J. Amer. Oil Chemists' Soc.*, 1948, **25**, 254; Swift, Brown, and O'Connor, *ibid.*, p. 39.
[22] Cf. Ellis, *J.*, 1950, 9.
[23] Hawkins, *J.*, 1955, 3288.

production of epoxide and acid occurs, followed in turn by hydroxyl groups. The epoxide concentration reaches a maximum and then decreases, whereas hydroxyl and acid concentrations continue to increase. The appearance and increase of acid can alternatively be shown by the intensity of the band at 3·18 μ, which provides a semiquantitative analysis, or by the bands at 5·81 and 5·85 μ. The acids, and in addition carbon dioxide, result from the further autoxidation of hydroperoxides.[24]

The method of formation of epoxides in the autoxidation of olefins is unknown. However, it is known that *cis*-olefins give a mixture of *cis*- and *trans*-epoxides, whereas *trans*-olefins give only *trans*-epoxides.[18] Isolated hydroperoxide, heated with a *cis*-olefin, gives an epoxide,[25] the reported properties of which indicate epoxidation by *cis*-addition to the double bond. As it was found that *cis*- and *trans*-epoxides do not isomerise under the conditions of an autoxidation and that the parent olefins do not undergo elaidinisation, it appears that the *trans*- and *cis*-epoxides are formed from *cis*-olefins by *two* concurrent reactions, *viz.*, (*A*) *cis*-epoxidation (by oxidation by the hydroperoxide molecule) and (*B*) a non-stereospecific two-step reaction. Route (*B*) involves in its first step the addition of a radical (such as $\cdot O_2H$ or $\cdot O_2R$) at one end of the double bond, giving a free radical in which rotation about the position of the original double bond can occur. In the second step, the epoxide ring is closed, after or simultaneously with rupture of the peroxide link in the radical. To explain the stereochemical result, this second step would have to yield exclusively the "*trans*"-compound (which is presumed to be the more stable isomer). The different stereochemical results for epoxide formation during the autoxidation of *cis*- and *trans*-olefins can thus be accommodated:




This dual mechanism would help to explain the high yields of epoxides [26] which can be obtained in the presence of alkali, under conditions where the amounts of hydroperoxide are too low to be compatible with the occurrence of epoxidation by direct attack of hydroperoxide. By route (*B*) only a small amount of hydroperoxide would suffice to initiate a chain reaction leading to extensive epoxide formation. Gasson, Millidge, Primavesi, Webster, and Young [26] explained this result by postulating that epoxidation proceeds by way of a moloxide [27] (I) but it is not apparent why this mode of reaction should not lead exclusively to *cis*-epoxidation. The eventual decrease in epoxide concentration, during olefin autoxidation, must be due to their ring-opening by water and acids [28] (present in the autoxidation products) to form free α-diol or its monoacyl derivative, since it was found that methyl *trans*-9 : 10- and *cis*-6 : 7-epoxystearate are both unaffected by gaseous oxygen at 120° in the presence of a uranium soap catalyst (cf. ref. 27). There was likewise no change if the epoxide esters were heated to that temperature by themselves or with an α-diol.

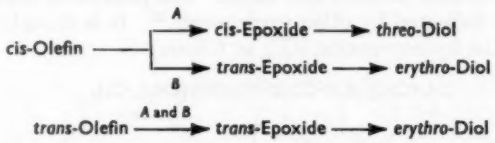


(I)

The infrared spectra of the pure *threo*- and *erythro*-isomers of both 9 : 10- and 6 : 7-dihydroxystearic acid were clearly distinguishable. The crude 9 : 10-dihydroxystearic acid, isolated from the autoxidation of methyl elaidate at 120°, gave a spectrum identical with that of pure *erythro*-9 : 10-dihydroxystearic acid, whilst the crude dihydroxy-acid, from the same reaction of methyl oleate, gave one showing it to be a mixture of *erythro*- with some

[24] Atherton and Hilditch, *J.*, 1944, 105.
[25] Swift and Dollear, *J. Amer. Oil Chemists' Soc.*, 1948, **25**, 52.
[26] Gasson, Millidge, Primavesi, Webster, and Young, *J.*, 1954, 2161.
[27] Paquot, *Bull. Soc. chim. France*, 1945, **12**, 120.
[28] Nicolet and Poulter, *J. Amer. Chem. Soc.*, 1930, **52**, 1186.

*threo*-isomer, *i.e.*, *cis*-olefin produces a mixture of *threo*- and *erythro*-diol, and a *trans*-olefin produces an *erythro*-diol only. Since long-chain epoxides undergo ring-opening with complete inversion [29] *cis*- and *trans*-epoxides would be the precursors of *threo*- and *erythro*-diols respectively. Thus the stereochemistry of the diols can be linked with the configurations of the epoxide products of the olefin autoxidations:




Methyl *threo*-9 : 10-dihydroxystearate was unchanged when heated alone or under the usual conditions of the autoxidation experiments. However, esterification occurred in the presence of compounds containing free carboxyl groups. Similarly, no oxidation took place when *threo*-9 : 10- or *erythro*-6 : 7-dihydroxystearic acid was treated with gaseous oxygen, the only changes being extensive intermolecular (and possibly some intramolecular) esterification: no epoxides or α-ketols were formed. The above accounts for the relatively large amounts of α-diols (approx. 10—15%) isolated, after hydrolysis, from the olefin-autoxidation product, and the high " additional ester " values obtained (66—102, *i.e.*, 2—3 times greater than can be explained on the assumption that the alkali is all used in hydrolysing monoacyl derivatives of dihydroxystearic acid).

The method of formation of α-ketols is unknown, though it has been shown that they are not obtained on autoxidation of α-diols. The α-ketol products undergo autoxidation themselves (which accounts for their low concentration in the end-products of olefin oxidation [1c]), the first isolable product being the α-diketone which is then itself oxidised to the scission acids. Thus, after reaction for 8·5 hr. at 120°, the following products were isolated from the autoxidation of lauroin (numbers refer to parts by wt. of product per 100 parts of lauroin): tetracontane-12 : 13-dione, 10; dodecanoic acid, 55; undecanal, 2·6; carbon dioxide, 0·7; lauroin (recovered), 20; water, a trace. The intermediate formation of the diketone could be followed in the infrared spectra of samples of the reaction mixture. These showed a continuous decrease of the alcoholic OH-stretching band at 3·0 μ, and the growth to a maximum intensity and then decrease of bands at 5·82, 10·85, and 13·79 μ. The last bands are characteristic of the spectrum of pure tetracontane-12 : 13-dione. They disappear entirely on prolonged oxidation, the spectrum becoming similar to that of pure lauric acid.

An analogous study of the autoxidation of a mixture of 6 : 7- and 7 : 6-hydroxyoxostearic acid was complicated by the formation of oils of high molecular weight as a result of polyesterification, indicating the ready esterification of α-ketols.

Since the above experiments showed the intermediate formation of α-diketones, autoxidation of some of these compounds was investigated. That of tetracontane-12 : 13-dione at 120° involved, during the early stages, the formation of a hydroperoxide (indicated by chemical analyses for active oxygen and by the infrared band at 2·9 μ) which reached its maximum concentration after about 2 hours and then diminished. Infrared spectra of successive samples indicated the disappearance of diketone (band at 13·79 μ) and the formation of carboxylic acid (bands at 3·1, 3·78, and 10·72 μ), the final spectrum closely resembling that of lauric acid. The chemical separation of the reaction product (after 9·5 hours' oxidation) gave (from 100 parts by wt. of starting material) dodecanoic acid, 60; undecanal, 5·7; carbon dioxide, 2·5; tetracontane-12 : 13-dione (recovered), 2·5; unidentified neutral oil, 15; and some water. The spectrum of the neutral oil suggests that it contains an enolic β-diketone grouping (bands at 2·91 and 6·1 μ).[12]

The autoxidation of methyl 9 : 10-dioxostearate (which is, accordingly, an intermediate

[29] Swern, *J. Amer. Chem. Soc.*, 1948, **70**, 1235.

XUM

in the autoxidation of methyl oleate and elaidate) again showed the formation of hydroperoxide during the early stages of reaction and the liberation of some carbon dioxide. The final product contained chiefly nonanoic and azelaic acid.

Analogous results have been reported for the monoketones, di*iso*propyl[30] and di-*n*-propyl ketone.[31] The former gave, in the course of autoxidation, some di*iso*propyl ketone hydroperoxide, butyric acid, acetone, and water. The position of chain scission (between CO and $CH_2$) is also indicated by other experiments.[32] It is thought therefore that the diketone reacts *via* the hydroperoxide, *e.g.*, as follows:

$$CH_3\cdot[CH_2]_{10}\cdot CO\cdot CO\cdot CH(O\cdot OH)\cdot[CH_2]_3\cdot CH_3$$

$$\downarrow$$

$$CH_3\cdot[CH_2]_{10}\cdot CO_2H + CO_2 + OHC\cdot[CH_2]_3\cdot CH_3$$

Water may be produced by decomposition of the hydroperoxide to an enolisable triketone.

This tentative scheme would explain the presence of all identified products and could be extended to other diketones.

The author acknowledges the help of Dr. V. Gold, of King's College, London, in all aspects of this work.

Acton Technical College, London, W.3. [*Received, August 7th,* 1957.]

[30] Sharp, Patton, and Whitcomb, *J. Amer. Chem. Soc.*, 1951, **73**, 5600.
[31] Sharp, Whitcomb, Patton, and Moorhead, *ibid.*, 1952, **74**, 1802.
[32] Jenkins, *ibid.*, 1935, **57**, 2733; Fuson and Jackson, *ibid.*, 1950, **72**, 1637.

---

## 189. 2 : 3-*Benzorubicene, Rubicene, and their Derivatives.*

By E. Clar and W. Willicks.

2 : 3-Benzorubicene (II) and its tetrahydro-derivative (III) have been obtained from the diol (I) in a sodium chloride–aluminium chloride melt; 2 : 3-6 : 7-dibenzofluoranthene (V) and its tetrahydro-derivative (VI) were obtained as by-products. A new synthesis of rubicene (X) is reported. *iso*Rubicene (XVI) has been resynthesised and its absorption spectrum compared with that of rubicene.

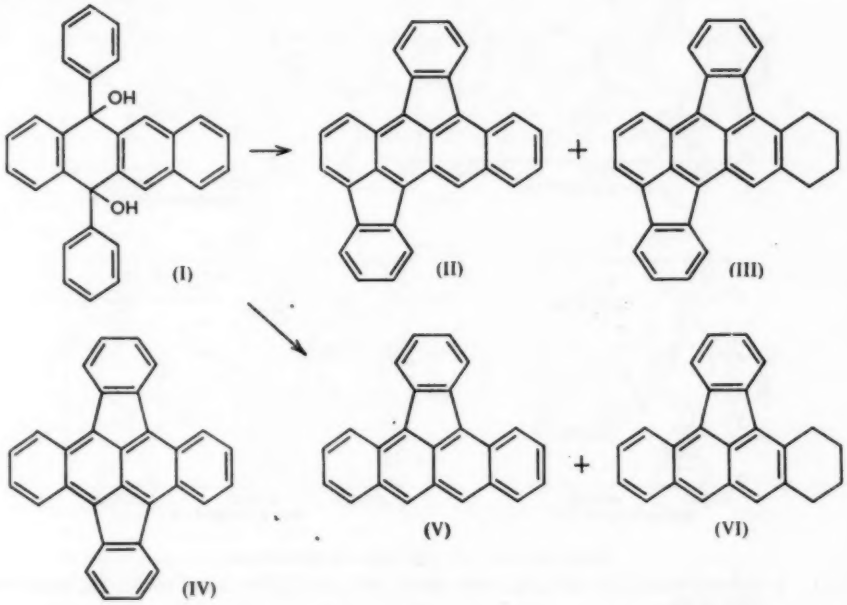
Clar and Stewart[1] reported that 5-phenyltetracene is cyclised to 2 : 3-6 : 7-dibenzofluoranthene (V) in an aluminium chloride melt. The same treatment converted the diol (I) into a deep blue hydrocarbon which differs from the di-*o*-phenylenetetracene (IV) of Dufraisse and Girard:[2] although the absorption spectra (Fig. 1) are very similar, the melting point of the new hydrocarbon is 215° the lower; we concluded therefore that our compound has structure (II) and this is supported by the fact that its tetrahydro-derivative (III) contains the aromatic skeleton of rubicene (X) as shown by comparison of the absorption spectra (Fig. 1).

Other by-products resulted by loss of one phenyl group from compound (I) and cyclisation of the other, to give 2 : 3-6 : 7-dibenzofluoranthene (V) and its tetrahydro-derivative[1] whose structure (VI) is proved by comparison of its absorption spectrum with that of 2 : 3-benzofluoranthene[3] (XI) (Fig. 3). Benzorubicene (II) adds maleic anhydride, to give a yellow adduct whose disodium salt has structure (VII), a conclusion reached by comparison of its spectrum with that of 4-phenylfluoranthene[4] (VIII) (Fig. 2).

Analogous results were obtained with the diol (IX). Fusion of this diol with sodium chloride–aluminium chloride melt gave rubicene (X) and, by loss of one benzene ring,

[1] Clar and Stewart, *J.*, 1952, 4783.
[2] Dufraisse and Girard, *Bull. Soc. chim. France*, 1934, **1**, 1359.
[3] Stubbs and Tucker, *J.*, 1951, 2939; Campbell and Marks, *J.*, 1951, 2941.
[4] von Braun and Manz, *Ber.*, 1937, **70**, 1603; Stubbs and Tucker, *J.*, 1950, 3288.

9-phenylanthracene and 2 : 3-benzofluoranthene [3] (XI; see Fig. 3). Besides these, a hydrocarbon of unknown structure was isolated which was also obtained by fusing rubicene with sodium chloride–aluminium chloride. *iso*Rubicene (XVI) was not isolated in this reaction.




Rubicene (X) was easily prepared from 1 : 5-dichloro-9 : 10-diphenylanthracene (XII) by means of potassium hydroxide in boiling quinoline. However, *iso*rubicene was not obtained by the same treatment of 1 : 4-dichloro-9 : 10-diphenylanthracene (XVII): short treatment gave 5-chloro-4-phenyl-2 : 3-benzofluoranthene (XVIII); further similar treatment of this compound did not yield *iso*rubicene but removed chlorine and afforded an alkali-soluble product.

Treating 1-chloro-9 : 10-diphenylanthracene (XV) with potassium hydroxide in boiling quinoline gave 4-phenyl-2 : 3-benzofluoranthene (XIV), in good yield, whose absorption spectrum is very close to that of 2 : 3-benzofluoranthene (XI) (see Fig. 3). Compound (XIV) gave rubicene and its further reaction products (see above) in a sodium chloride–aluminium chloride melt, but no *iso*rubicene.

We have repeated Fedorov's synthesis [5] of *iso*rubicene (XVI) and obtained a very small yield of a hydrocarbon with the properties reported by him. However, the absorption spectrum of our *iso*rubicene is very different from that reported by Setkina and Fedorov [6] (see Fig. 4), being similar to that of rubicene (X) (Fig. 4). However, the relationship is not as close as in the case of 2 : 3-benzorubicene (II) and di-*o*-phenylenetetracene (VI) (Fig. 1).

## Experimental

M. p.s were taken in evacuated capillaries. Microanalyses are by Mr. J. M. L. Cameron and Miss M. W. Christie.

The tetracene was supplied by Messrs. Shore Transit Co. Ltd., 80, Wolmer Gardens, Edgware, Middlesex. The tetracenequinone was prepared by oxidation with chromic acid in acetic acid.

[5] Fedorov, *Bull. Acad. Sci. U.R.S.S., Classe sci. Chim.*, 1947, 397; *Chem. Abs.*, 1948, 1585.
[6] Setkina and Fedorov, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1949, 545; *Chem. Abs.*, 1950, **44**, 1333.

XUM

FIG. 1.

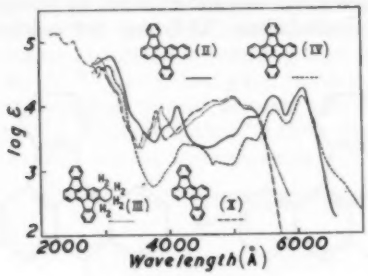



FIG. 2.

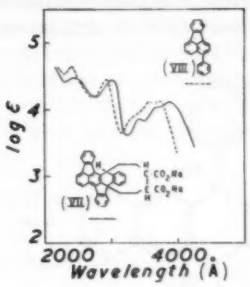



FIG. 3.

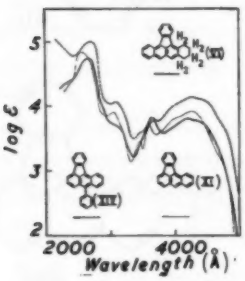
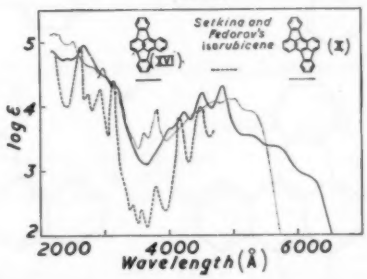



FIG. 4.




*Absorption max.* (Å) *and* log ε (*in parentheses*).

FIG. 1. 2 : 3-*Benzorubicene* (II) *in* $C_6H_6$: 6100 (4·26), 5650 (4·14), 5300 (3·80), 4960 (3·52), 4140 (3·99), 3100 (4·80).
5 : 6-11 : 12-*Di-o-phenylenetetracene* (IV) *in* $C_6H_6$: 6090 (4·14), 5620 (3·92), 5220 (3·48), 4200 (3·40), 3050 (4·64), 2900 (4·63).
*Rubicene* (X) *in* $C_6H_6$: 5300 (3·82), 4940 (4·00), 4650 (3·95), 3790 (3·77), 3600 (3·45), 2970 (4·85); *in* EtOH, 2510 (5·00), 2300 (5·10).
1′ : 2′ : 3′ : 4′-*Tetrahydro*-2 : 3-*benzorubicene* (III) *in* $C_6H_6$: 5230 (3·98), 4980 (4·09), 4680 (4·00), 3870 (3·98), 3700 (3·64), 2910 (4·76).

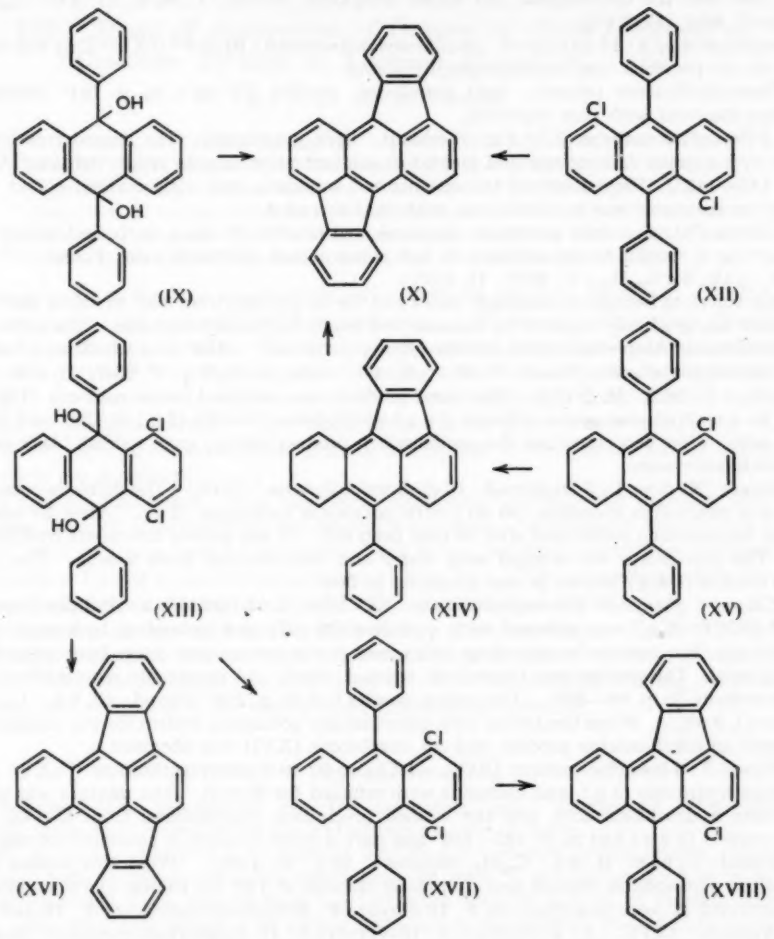
FIG. 2. *Disodium salt of the maleic anhydride adduct* (VII) *in* EtOH: 3850 (4·18), 3670 (4·04), 3420 (3·76), 3030 (4·42), 2460 (4·45).
4-*Phenylfluoranthene* (VIII) *in* EtOH: 3700 (4·20), 3580 (4·18), 3145 (3·81), 2940 (4·45), 2405 (4·62).

FIG. 3. 1′ : 2′ : 3′ : 4′-*Tetrahydro*-2 : 3-6 : 7-*dibenzofluoranthene* (VI) *in* EtOH: 4250 (3·81), 3700 (3·78), 2660 (4·74).
4-*Phenyl*-2 : 3-*benzofluoranthene* (XIV) *in* EtOH: 4300 (4·13), 3660 (3·80), 3100 (4·06), 2700 (5·00).
2 : 3-*Benzofluoranthene* (XI) *in* EtOH: 4280 (3·92), 3630 (3·70), 3460 (3·46), 3080 (3·90), 2560 (4·85).

FIG. 4. iso*Rubicene* (XVI) *in* $C_6H_6$: 6250 (2·87), 5630 (3·37), 5300 (3·54), 4850 (4·31), 4530 (4·20), 4250 (3·90), 4020 (3·66), 3170 (4·34); *in* EtOH: 2680 (4·97).
*Setkina and Fedorov's* iso*rubicene*: [6] 4480 (4·00), 4150 (3·93), 3800 (2·81), 3600 (2·60), 3450 (2·66), 3150 (4·20), 2950 (4·10), 2760 (4·01), 2650 (4·63).
*Rubicene* (X) *in* $C_6H_6$: 5300 (3·92), 4940 (4·00), 4650 (3·95), 3790 (3·77), 3600 (3·45), 2970 (4·85); *in* EtOH: 2510 (5·00), 2300 (5·10).

*Condensation of Diol* (I).—5 : 12-Dihydro-5 : 12-diphenyltetracene-5 : 12-diol (I) was obtained from tetracenequinone and phenyl-lithium in good yield.[7] It (5 g.) was added with stirring within 5 min. to a melt of sodium chloride (10 g.) and aluminium chloride (50 g.) at 120°. The melt was decomposed with dilute hydrochloric acid, and the precipitate filtered off, washed with hot water, and treated with aqueous ammonia. The dried black condensation product

[7] Cf. Dufraisse and Horclois, *Bull. Soc. chim. France*, 1936, **3**, 1894, 1899; Allen and Gilman, *J. Amer. Chem. Soc.*, 1936, **58**, 937; 1940, **62**, 2408.




(4 g.) was chromatographed on alumina, elution being with light petroleum with increasing proportions of benzene. The hydrocarbons were eluted in the following order:

1′ : 2′ : 3′ : 4′-Tetrahydro-2 : 3-6 : 7-dibenzofluoranthene (VI) (9 : 1 light petroleum–benzene), yellow needles (120 mg.), m. p. and mixed m. p. 150°.

2 : 3-6 : 7-Dibenzofluoranthene (V) (4 : 1 light petroleum–benzene), red needles (25 mg.) which after recrystallisation from xylene had m. p. and mixed m. p. (ref. 1) 215°.

1′ : 2′ : 3′ : 4′-*Tetrahydro*-2 : 3-*benzorubicene* (III) (1 : 1 light petroleum–benzene), reddish-brown needles (85 mg.), m. p. 182°, dissolving in concentrated sulphuric acid to give an orange solution changing to green (Found: C, 95·0; H, 5·1. $C_{30}H_{20}$ requires C, 94·7; H, 5·3%).

2 : 3-*Benzorubicene* (II) (eluant: benzene): the main fraction was violet and yielded deep blue needles (450 mg.), m. p. 250°, dissolving to a deep green solution in concentrated sulphuric acid; the blue solution in benzene showed an intense red fluorescence (Found: C, 95·4; H, 4·4. $C_{30}H_{16}$ requires C, 95·7; H, 4·3%).

*Maleic Anhydride Adduct* (VII; Fig. 2) *of* 2 : 3-*Benzorubicene*.—Benzorubicene (20 mg.) and maleic anhydride (20 mg.) were refluxed for 30 min. in xylene (20 ml.). The blue solution became yellow. The *adduct* crystallised on concentration. The crystals decomposed gradually

above 300° into the hydrocarbon and maleic anhydride (Found: C, 85·2; H, 4·6. $C_{34}H_{18}O_3$ requires C, 86·0; H, 3·8%).

*Condensation of* 9 : 10-*Dihydro*-9 : 10-*diphenylanthracene*-9 : 10-*diol* [8] (IX).—This was carried out as in the previous case, chromatography giving:

9-Phenylanthracene (eluant : light petroleum), needles (75 mg.), m. p. 154° (absorption spectrum identical with that reported).

2 : 3-Benzofluoranthene (XI; Fig. 3) (eluant: light petroleum): The second fraction was yellow with a green fluorescence and yielded on concentration orange-yellow needles (15 mg.), m. p. 143—145°. They dissolved in concentrated sulphuric acid with a violet colour. The absorption spectrum was in accordance with that recorded.[1]

Rubicene (X) (4 : 1 light petroleum–benzene), red needles (50 mg.), m. p. and mixed m. p. 303°, giving a reddish-brown solution in hot concentrated sulphuric acid (Found: C, 95·5; H, 4·5. Calc. for $C_{26}H_{14}$: C, 95·7; H, 4·3%).

Later fractions became increasingly violet and the m. p.s rose from 300° to above 450° when the eluant was gradually replaced by benzene and finally by trichlorobenzene. The latter gave on concentration deep violet-black needles (60 mg.), decomp. >455° (red solution in hot concentrated sulphuric acid) (Found: C, 95·7; H, 4·0. Calc. for $C_{26}H_{14}$: C, 95·7; H, 4·3. Calc. for $C_{26}H_{12}$: C, 96·3; H, 3·7%). The same product was obtained when rubicene (1 g.) was added to a melt of aluminium chloride (10 g.) and sodium chloride (2 g.) at 130° and heated for 15 min.; after decomposition the condensation product (0·6 g.) gave reddish-black needles from trichlorobenzene.

*Rubicene* (X) *from* 1 : 5-*Dichloro*-9 : 10-*diphenylanthracene* [9] (XII).—The dichloro-compound (2 g.) was refluxed in quinoline (50 ml.) with potassium hydroxide (2 g.). After 10 min. the mixture became deep yellow and after 30 min. deep red. It was poured into dilute hydrochloric acid. The precipitate was washed with water and recrystallised from xylene. The bright yellow needles (1·4 g.) had m. p. and mixed m. p. 304°.

5-*Chloro*-4-*phenyl*-2 : 3-*benzofluoranthene* (XVIII).—1 : 4-Dichloro-9 : 10-diphenylanthracene [10] (XVII) (2 g.) was refluxed with quinoline (20 ml.) and potassium hydroxide (2 g.). After 10 min. the mixture became deep yellow and it was poured into dilute hydrochloric acid after 15 min. The *product* was filtered off, washed, dried, and repeatedly recrystallised from light petroleum (b. p. 60—80°). The yellow needles had m. p. 215° (Found: Cl, 9·9. $C_{26}H_{15}Cl$ requires Cl, 9·8%). When treatment with quinoline and potassium hydroxide was considerably prolonged an alkali-soluble product and no *iso*rubicene (XVI) was obtained.

4-*Phenyl*-2 : 3-*benzofluoranthene* (XIV).—1-Chloro-9 : 10-diphenylanthracene [10] (XV) (3 g.), potassium hydroxide (3 g.), and quinoline were refluxed for 30 min. The mixture was poured into dilute hydrochloric acid, and the washed precipitate recrystallised from alcohol. The yellow leaflets (2·2 g.) had m. p. 185—186° and gave a green solution in concentrated sulphuric acid (Found: C, 94·8; H, 5·1. $C_{26}H_{16}$ requires C, 95·1; H, 4·9%). When this *product* (XIV) was melted with sodium chloride and aluminium chloride at 120° for 10 min. the same products were obtained as were described for 9 : 10-dihydro-9 : 10-diphenylanthracene-9 : 10-diol (IX).

iso*Rubicene* (XVI).—1 : 4-Dichloro-9 : 10-dihydro-9 : 10-diphenylanthracene-9 : 10-diol [10] (XVII) (1 g.), dry oxalic acid (12 g.), sodium acetate (3 g.), copper powder (0·3 g.), and aluminium powder (0·3 g.) were heated at 30 mm. for 30 min. to 300° and then for one hour to 360°. The mixture was extracted with hot water and then with benzene (15 ml.). The dried benzene solution was chromatographed on alumina, with light petroleum as eluant which was gradually replaced by benzene. The first fraction gave dichlorodiphenylanthracene (XVII) (50 mg.), m. p. 178°; the next fraction was 5-chloro-4-phenyl-2 : 3-benzofluoranthene (XVIII) (200 mg.), m. p. 214°; and the third fraction (obtained by pure benzene) gave reddish-brown needles (10 mg.), m. p. 279°, of *iso*rubicene (Found: C, 95·7; H, 4·4. Calc. for $C_{26}H_{14}$: C, 95·7; H, 4·3%).

The authors thank Professor Dufraisse for a sample of 5 : 6-11 : 12-di-*o*-phenylenetetracene, and the British Council for a maintenance grant (to W. W.).

Department of Chemistry, The University of Glasgow. [*Received, August 28th,* 1957.]

[8] Haller and Guyot, *Compt. rend.*, 1904, **138**, 1251; *Bull. Soc. chim. France*, 1904, **31**, 795.

[9] Barnett, Cook, and Wiltshire, *J.*, 1927, 1724; Fedorov, *Bull. Acad. Sci. U.R.S.S., Classe sci. Chim.*, 1947, 397.

[10] Dufraisse and Velluz, *Bull. Soc. chim. France*, 1942, **9**, 186; Fedorov, *Bull. Acad. Sci. U.R.S.S., Classe sci. Chim.*, 1947, 397.

XUM

## 190. *Heats of Adsorption of Oxygen on Solid Solutions of Uranium Dioxide in Thorium Dioxide at −183°.*

By J. D. M. McConnell.

By use of a " cyclone microniser ", specimens of solid solutions containing 20 mole % and 10 mole % of uranium dioxide in thorium dioxide have been prepared having surface areas of about 12 m.²/g. The initial heat of adsorption of oxygen on these solid solutions at −183° falls as the uranium content is decreased. A slow evolution of heat at partial coverage has been observed, but differs from that noted earlier on pure uranium dioxide.

During a study of the heat of adsorption of oxygen on uranium dioxide at −183°,[1] some work was carried out on a solid solution consisting of 75 moles % of uranium dioxide and 25 mole % of thorium dioxide. Firing at a high temperature is essential in preparation of such solid solutions,[2,3] but yields a product having a small surface area (large particle size). At −183°, the reaction of oxygen is confined to the surface of uranium dioxide or its solid solutions in thorium dioxide. The small surface areas cause small uptakes of oxygen, and measurement of the differential heat of adsorption of oxygen by means of small increments of gas is difficult.

A " cyclone microniser " has now been developed[4] suitable for handling the small quantities in which solid solutions are generally available. Whereas previously the surface areas of solid solutions were of the order of 0·2 m.²/g., products have been obtained from the microniser having surface areas in excess of 10 m.²/g. This has made possible the study of heats of adsorption of fairly dilute solid solutions of uranium dioxide.

Previous studies on oxides having high surface areas have frequently been carried out on material treated at relatively low temperatures and thus of somewhat dubious composition. The present materials differ from the well-characterised starting material only in having been subjected to the purely physical process of grinding.

### Experimental

*Calorimeter.*—The calorimeter was the instrument used previously.[1] The operation, including the method of evaluating heats of adsorption, was as before.

*Solid Solutions.*—Starting from thorium dioxide and hydrated uranyl nitrate, solutions in nitric acid were prepared containing respectively 20 mole % of uranium with 80 mole % of thorium (specimen TL8), and 10 mole % of uranium with 90 mole % of thorium (specimen TL9). The precipitate obtained by adding ammonia to the solution was dried in air at 150°, then heated in air at 900°. The product was ground in an agate mortar. *X*-Ray photographs confirmed that the products were single-phase.

*Microniser.*—The cyclone microniser, described in detail elsewhere,[4] consists of a loop of Pyrex glass tubing in the vertical plane round which the solid sample is blown by means of compressed air. After leaving the loop, the solid is crudely " fractionated " according to particle size in three separators in series. The surface area (measured by the B.E.T. method, with nitrogen at −195°) of specimen TL8 from the second separator was 11·7 m.²/g.; that of specimen TL9, also from the second separator, was 12·7 m.²/g. The silica contents of these specimens were 500 p.p.m.

Immediately before the calorimetric measurements, the specimens were reduced in static carbon monoxide at 600°/1 atm. for 1 hr., and transferred to the calorimeter *in vacuo*, this being chosen to minimise deposition of carbon on the oxide surface.[5]

[1] Ferguson and McConnell, *Proc. Roy. Soc.*, 1957, *A*, **241**, 67.
[2] Roberts, *J.*, 1954, 3332.
[3] McConnell and Roberts in "Chemisorption," (Chem. Soc. Symp.), July, 1956, Butterworths, London, 1957.
[4] McConnell, A.E.R.E., C/M 319.
[5] Roberts, Walter, and Wheeler, to be published.

XUM

## Results and Discussion

The change in differential heat of adsorption with uptake of oxygen by the oxide surface is shown in Fig. 1. The uptake of oxygen (expressed in terms of the " chemisorption limit " as defined by Roberts [2]) varies with the uranium content of the solid solution and, from Roberts's work, is 12% of $V_m$ (the monolayer volume) for the 20% solid solution, and 6% of $V_m$ for the 10% solid solution. On this basis, the coverages quoted in Fig. 1 and in the Table of several times the chemisorption limit still signify an uptake of less than a monolayer referred to the *total* solid surface.

Fig. 1 shows a steady decrease in the heat of adsorption with uptake of oxygen, as with pure uranium dioxide. The initial heat of adsorption decreases as the uranium content of

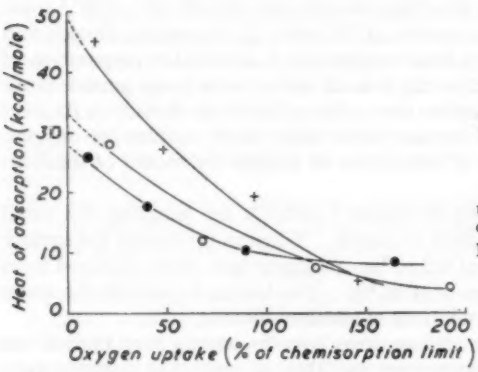



Fig. 1. *Change of heat of adsorption with surface coverage.*

Symbols refer to composition (mole % of uranium): + 75%, ○ 20%, ● 10%. (Results on the 75% solid solution are included for comparison.)

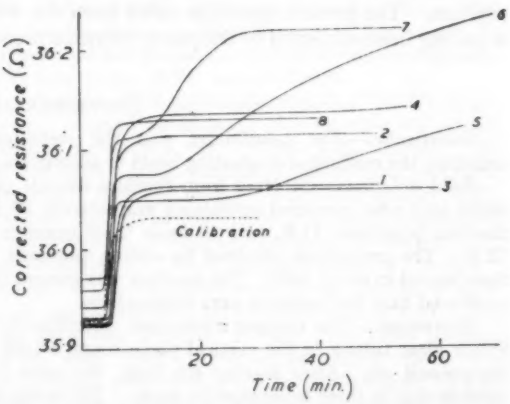



Fig. 2. *Corrected cooling curves for specimen TL9.*

the solid solution is reduced. It might have been expected that the true initial heat of adsorption, measured on an infinitely small increment, would be the same as on pure uranium dioxide, but that the rate of decrease of heat of adsorption with coverage would be greater on the solid solution. In these more dilute solid solutions, however, each uranium atom is in an environment composed largely of thorium atoms. Thus any process, such as the chemisorption of oxygen, which involves electron transfer will take place less readily on the solid solution than on pure uranium dioxide. The effect of diluting the uranium with " inert " thorium will be the more marked the more it involves the bulk of the uranium atoms and the less it is characteristic of individual atoms.

Corrected cooling curves (see ref. 1) are shown in Fig. 2 for specimen TL9. Up to about

200% of the chemisorption limit (see also the Table), heat is evolved rapidly, and Newtonian cooling is established within less than 20 min., as in electrical calibration. Above 200% of the chemisorption limit, Newtonian cooling appears to be established, to be followed (curves 5—7, Fig. 2) by a further slow evolution of heat.

| Specimen | Increment | $O_2$ adsorbed (mmoles) incremental | $O_2$ adsorbed (mmoles) total | Total coverage (% chemisorption) | Heat of adsorption (kcal./mole) |
|---|---|---|---|---|---|
| TL8 | 1 | 0·0604 | 0·0604 | 44 | 28·3 |
| | 2 | 0·0678 | 0·1282 | 93 | 12·1 |
| | 3 | 0·0915 | 0·2197 | 159 | 7·7 |
| | 4 | 0·0970 | 0·3167 | 229 | (8·1) 4·5 |
| | 5 | 0·1118 | 0·4285 | 310 | — |
| | 6 | 0·1279 | 0·5564 | 410 | 4·1 |
| TL9 | 1 | 0·0124 | 0·0124 | 22 | 26·1 |
| | 2 | 0·0241 | 0·0365 | 64 | 17·9 |
| | 3 | 0·0305 | 0·0670 | 118 | 10·6 |
| | 4 | 0·0541 | 0·1211 | 214 | 8·8 |
| | 5 | 0·0623 | 0·1834 | 324 | (11·0) 4·4 |
| | 6 | 0·0784 | 0·2618 | 460 | (9·2) 4·0 |
| | 7 | 0·0940 | 0·3558 | 630 | 6·4 3·7 |
| | 8 | 0·1090 | 0·4648 | 820 | 3·4 |

Monolayer volumes: TL8, 1·152 mmoles. TL9, 0·945 mmole.

This slow evolution differs from the slow reaction on pure uranium dioxide in two main respects. First, the second evolution of heat is very slow in increment 5, rather less so in increment 6 (and in neither of these increments was final establishment of Newtonian cooling observed), and complete after about 35 min. in increment 7. This is a reversal of the behaviour on pure uranium dioxide, where the slow reaction becomes increasingly slow with coverage. Secondly, it has been shown [2] that the chemisorption limit corresponds to reaction of oxygen with about half of the surface uranium sites. If all the surface uranium sites were to react, oxygen would be adsorbed up to 200% of the chemisorption limit. The further chemisorption of oxygen on a solid solution must involve the thorium atoms (since reaction with uranium atoms in the bulk of the solid at −183° is ruled out by arguments summarised elsewhere [6]), and the present slow evolution of heat must be a reaction of thorium atoms in the surface.

Heats of adsorption (3·5—4·5 kcal./mole) evaluated from the first parts of curves 5—7 for TL9 and curve 4 for TL8 are typical of physical adsorption. It has not been possible to evaluate accurate heats from the second parts of curves 5 and 6, but estimated heats are given in parentheses in the Table. (An estimated value is also quoted for increment 4 on specimen TL8.) Although these heats are low compared with values normally considered typical of chemisorption, they are nevertheless higher than the highest possible value (~5 kcal./mole) for physical adsorption. Very low heats of chemisorption have also been inferred from magnetic measurements on nickel on which hydrogen had been adsorbed.[7] Low-energy chemisorption has been discussed by Dowden.[8]

Whatever the significance of the slow evolution of heat at higher surface coverages of the solid solutions, the heats calculated from the first parts of two-part curves suggest that the first stage in the uptake of oxygen by the oxide is physical adsorption. An increasing body of evidence suggests that physical adsorption frequently, if not even always, precedes chemisorption. Changes in the resistance of evaporated nickel films have been interpreted as indicating that a considerable fraction of the total water vapour or carbon dioxide adsorbed is first attached to the surface in the physically adsorbed state.[9] Again, the behaviour of physically adsorbed molecules has been considered to depend on the relative values of two activation energies, one for desorption and the other for incorporation into

[6] Anderson, Roberts, and Harper, *J.*, 1955, 3946.
[7] Selwood, *J. Amer. Chem. Soc.*, 1956, **78**, 3893.
[8] Dowden in "Chemisorption," (Chem. Soc. Symp.), July, 1956, Butterworths, London, 1957.
[9] Suhrmann and Wedler, *Z. physikal. Chem.* (*Frankfurt*), 1957, **10**, 184.

the chemisorbed state.[10] (A somewhat similar picture has been invoked to explain the slow reaction observed on pure uranium dioxide.[1]) Evidence for a two-stage reaction has also been deduced from results on the adsorption of nitrogen on tungsten.[11]

It must be emphasised that although both pure uranium dioxide and solid solutions of uranium and thorium dioxides exhibit slow reactions and heats of low-energy chemisorption, these reactions must be quite different. In the former case, uranium sites must obviously be involved, whereas in the latter they cannot be.

The author thanks Dr. L. E. J. Roberts for many helpful discussions, and for criticism of this paper.

ATOMIC ENERGY RESEARCH ESTABLISHMENT,
HARWELL, NR. DIDCOT, BERKS. [*Received, September 25th*, 1957.]

[10] Ehrlich, *J. Phys. Chem.*, 1955, **59**, 473.
[11] *Idem, J. Chem. Phys.*, 1955, **23**, 1543.

---

## 191. *Researches on Acetylenic Compounds. Part LIX.* The Synthesis of Three Polyacetylenic Antibiotics.*

By P. J. ASHWORTH, E. R. H. JONES, G. H. MANSFIELD, K. SCHLÖGL, J. M. THOMPSON, and M. C. WHITING.

Syntheses of the antibiotics "diatretyne-I," "diatretyne-II," and "agrocybin" are described. In each case a cross-coupling reaction between an appropriate derivative of propiolic acid and a $C_6$ component was employed.

DIATRETYNE-I was first isolated from culture fluids of the Basidiomycete fungus *Clitocybe diatreta* by Anchel,[1] and was shown [2] to be a monoamide of an acid of type (I). A sample kindly sent to us was found to absorb intensely at 960 cm.$^{-1}$, but not at *ca.* 800 cm.$^{-1}$; it was

(I) $HO_2C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2H$ $H_2N{\cdot}CO{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}\underset{trans}{CH{=}CH}{\cdot}CO_2H$ (II)

therefore one of the two *trans*-isomers.[3] Potentiometric titration gave a p$K_a$ value of about 3·55, and reference to data obtained for a range of related acids [4] established its structure as (II) since, for all αβ-acetylenic acids studied, p$K$ values below 2·7 were found.

Synthetical confirmation could most obviously be obtained by a mixed-coupling technique in this instance, employing the ester or amide of propiolic acid as one component and pent-2-en-4-ynoic acid as the other. Methyl propiolate, however, was found by Christensen and Sørensen [5] to behave abnormally under the usual coupling conditions, giving two products of high oxygen content, the structures of which remain unknown.

*trans*-Pent-2-en-4-ynoic acid was first shown to couple normally; then the cross-coupling reaction between pentenynoic acid and methyl propiolate was found to give a small yield of the desired half-ester, provided that a low temperature was maintained. Brief treatment with ammonia converted this into a half-amide which showed ultraviolet and infrared spectra identical with those of diatretyne-I and like the latter gave suberamic acid on hydrogenation. The biological activity of the synthetic sample, however, was lower than that observed for specimens of the natural compound, a result which was traced to the presence of small amounts of diatretyne-II in existing specimens of the latter.[6]

Diatretyne-II, first isolated from the same cultures as diatretyne-I, was later

* Part LVIII, *J.*, 1957, 4633.

[1] Anchel, *J. Amer. Chem. Soc.*, 1952, **74**, 1588.
[2] *Idem, ibid.*, 1953, **75**, 4621.
[3] Allan, Meakins, and Whiting, *J.*, 1955, 1874.
[4] Mansfield and Whiting, *J.*, 1956, 4761.
[5] Christensen and Sørensen, *Acta Chem. Scand.*, 1952, **6**, 893.
[6] Anchel, personal communication.

shown to be the corresponding nitrile; [7] it was, indeed, obtained in minute yield by the dehydration of diatretyne-I and identified by its biological activity,[7] in which it far surpasses the amide. For the latter reason an effective synthesis was the more desirable. However, propiolonitrile failed to give a detectable quantity of cross-coupling products with the acetylenes tested under the usual conditions. The method used by Brockman [8] in the direct oxidative coupling of propiolonitrile, *i.e.*, the action of potassium ferricyanide on the precipitated cuprous derivative, was therefore employed. *trans*-Pent-2-en-4-yn-1-ol was used as the second component, and the desired 7-cyanohept-2-en-4 : 6-diyn-1-ol (III)

$$HO{\cdot}CH_2{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}Cu\downarrow + Cu\downarrow{\cdot}C{\equiv}C{\cdot}CN \longrightarrow HO{\cdot}CH_2{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CN \quad (III)$$

$$\downarrow$$

$$HO_2C{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CN \quad (IV)$$

was obtained in 14% yield. This proved to be a powerful vesicant (weaker irritant properties are common among acetylenic nitriles). Oxidation with chromic acid and sulphuric acid in acetone gave the corresponding acid, which showed ultraviolet absorption maxima in exact agreement with those recorded for diatretyne-II [7] * (Fig. 1).

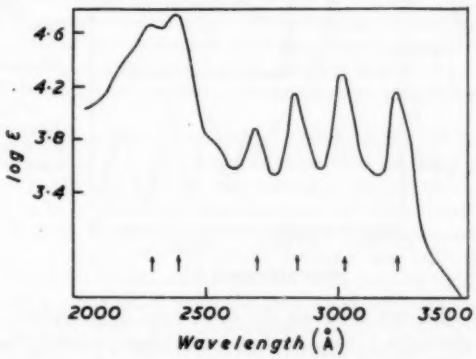



FIG. 1. *Absorption spectrum of diatretyne-II in alcohol.*

—— *Synthetic acid* (IV). *Arrows denote absorption maxima given by Anchel.*[1]

Agrocybin was first isolated from culture fluids of the Basidiomycete fungus *Agrocybe dura* by Kavanagh, Hervey, and Robbins.[9] It was subsequently shown to be converted by hydrogenation over platinum into octanamide; and octa-2 : 4 : 6-triynamide was suggested as its structure.[10] This compound was then synthesised ; [11] the infrared spectrum lacked a few strong bands present in that of the natural compound, but the ultraviolet spectrum showed almost exact agreement. When alkali was added, however, the synthetic amide and the antibiotic reacted, under similar conditions, at quite different rates. In each case the spectrum became more intense and moved to longer wavelengths, but the new product, or products, obtained showed a much sharper fine structure at rather shorter wavelengths in the case of the synthetic amide (Fig. 2). Thus it became clear that

* No intensity data were published for diatretyne-II, and it has not yet been possible to compare the infrared spectrum or the biological activity of the cyano-acid (IV) with those of the antibiotic; proof of identity is thus less complete than for the other polyacetylenic antibiotics. It was, however, possible to prepare from nudic acid B (Florey, Chain, Heatley, Jennings, Sanders, Abraham, and Florey, "Antibiotics," Oxford Univ. Press, 1949, p. 385; Heatley and Stephenson, *Nature*, 1957, **179**, 1078) and from the acid (IV) identical methyl esters (infrared and ultraviolet spectra and mixed melting point), so that the identity of our acid (IV) and nudic acid B is completely established. The spectrum shown in Fig. 1, although superficially similar to those of other polyynes, actually differs significantly from that of any other chromophoric system yet published in the positions of the maxima.

[7] Anchel, *Science*, 1955, **121**, 607.
[8] Brockman, *Canad. J. Chem.*, 1955, **33**, 507.
[9] Kavanagh, Hervey, and Robbins, *Proc. Nat. Acad. Sci. Washington*, 1950, **36**, 102.
[10] Bu'Lock and Jones, *J.*, 1953, 3719.
[11] Jones, Thompson, and Whiting, *J.*, 1957, 2012.

XUM

agrocybin is not octa-2 : 4 : 6-triynamide; and, by elimination, 8-hydroxyocta-2 : 4 : 6-triynamide became the most plausible structure. Its synthesis was attempted by cross-coupling methyl propiolate with penta-2 : 4-diyn-1-ol using cuprous chloride, ammonium chloride, and hydrogen peroxide [12] at low temperatures. The expected hydroxy-ester was obtained as a solid, though only in 5% yield. Its reaction with ammonia to give the amide was virtually complete after a few minutes at −5°; more normal reaction conditions led apparently to addition, the required amide being lost. The amide showed ultraviolet and infrared spectra identical with those of agrocybin, and reacted with ethanolic sodium

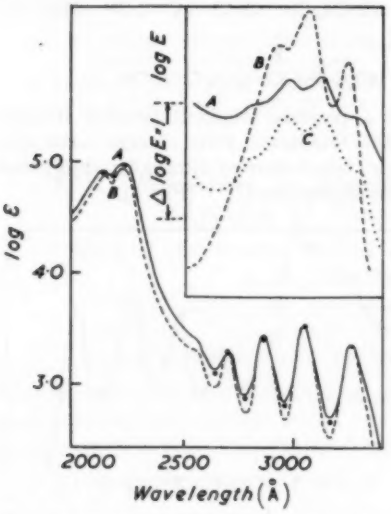



FIG. 2. *Absorption spectrum of agrocybin in alcohol.*

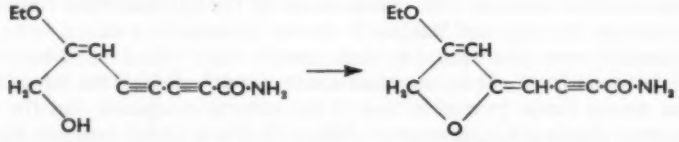
*Main diagram: A* (——), *Synthetic* 8-*hydroxyocta-2 : 4 : 6-triynamide; B* (– – –), *synthetic octa-2 : 4 : 6-triynamide; C* (. . .), *agrocybin (maxima and minima only).*

*Inset: A, Synthetic* 8-*hydroxyoctatriynamide; B, synthetic octa-2 : 4 : 6-triynoamide; C, agrocybin.*

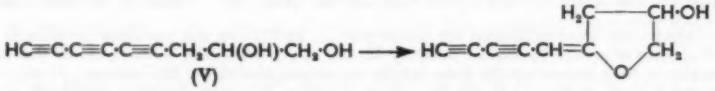
*All spectra are for dilute solutions previously treated with a catalytic quantity of sodium hydroxide solution.*

(The wavelength-scale applies also to the inset; and although the optical densities are arbitrary, the logarithmic increment is the same in the three spectra and the same as that in the main diagram.)

hydroxide at about the same rate as the latter, giving products with the same absorption spectrum. As a final proof of identity, distribution coefficients between water–ether and water–ethyl acetate were determined.[13]




The difference between the spectra of the ethanol-adducts of 8-hydroxyoctatriynamide and of the simple amide requires explanation. Probably the first product is formed by addition at $C_{(7)}$ in each case; [14] the agrocybin derivative will then be able to cyclise to a




compound which would be expected to absorb at longer wavelengths, and with less sharp fine structure, than the initial product. Such intramolecular nucleophilic additions take place much more readily than the corresponding intermolecular reactions [15] and are clearly involved in the alkali-catalysed transformation of biformin (V).[16] Superficially the

[12] Milas and Mageli, *J. Amer. Chem. Soc.*, 1953, **75**, 5971.
[13] Bu'Lock, Jones, Mansfield, Thompson, and Whiting, *Chem. and Ind.*, 1954, 900.
[14] Bohlmann and Viehe, *Chem. Ber.*, 1955, **88**, 1017.
[15] See, *inter al.*, Eglinton, Jones, and Whiting, *J.*, 1952, 2873.
[16] Anchel and Cohen, *J. Biol. Chem.*, 1954, **208**, 319; see Bu'Lock, *Quart. Rev.*, 1956, **10**, 386.

XUM

effects, upon absorption spectra, of such processes may resemble those observed in the isomerisations of acetylenic-allenic antibiotics, which have recently been reviewed.[17]

*Light-absorption maxima for compounds,* R·[C≡C]$_3$·COX, *in ethanol.*

| R = $CH_2$·OH, X = OMe | | R = $CH_2$·OH, X = OMe | | R = $CH_2$·OH, X = $NH_2$ | | R = $CH_2$·OH, X = $NH_2$ | |
|---|---|---|---|---|---|---|---|
| Å | $10^{-3}\varepsilon$ | Å | $10^{-3}\varepsilon$ | Å | $10^{-3}\varepsilon$ | Å | $10^{-3}\varepsilon$ |
| 3295 | 2·1 | 2260 | 82 | 3260 | 2·25 | 2700 | 2·0 |
| 3080 | 3·65 | 2180 | 75·5 | 3045 | 3·45 | 2240 | 100 |
| 2890 | 3·0 | | | 2865 | 2·85 | 2150 | 84 |
| 2725 | 1·8 | | | | | | |
| 2580 | 1·0 | | | | | | |

## Experimental

Precautions necessary for work with unstable polyacetylenes have been outlined previously;[18] they were needed especially for the triacetylenes related to agrocybin.

### *Diatretyne*-I

trans : trans-*Deca*-2 : 8-*diene*-4 : 6-*diynedioic Acid*.—*trans*-Pent-2-en-4-ynoic acid (1·65 g.) in acetone (10 c.c.) was added to a solution of cuprous chloride (4 g.) and ammonium chloride (14 g.) in water (20 c.c.). The mixture was stirred in an atmosphere of oxygen until absorption was complete, the temperature being held at 5° by external cooling. Phosphoric acid (20 c.c.; 50%) was added, and the precipitate was collected and extracted with potassium hydroxide solution; reprecipitation and crystallisation from methanol gave the dicarboxylic acid (1·6 g.), which decomposed, when heated, without melting but showed light-absorption properties similar to those recorded by Heilbron *et al.*[19]

7-*Methoxycarbonylhept*-2-*ene*-4 : 6-*diynoic Acid*.—(*a*) Methyl propiolate (2·0 g.) and pent-2-en-4-ynoic acid (2·0 g.) in acetone (10 c.c.) were added to a mixture of cuprous chloride (10 g.), ammonium chloride (16 g.), and water (30 c.c.), and the solution was stirred in oxygen at *ca.* 5° until absorption was complete (1020 c.c. in 15 hr.). The resultant suspension of basic cupric salts was extracted with ether, without any attempt to filter it, which previous experience has shown to be impracticable and unnecessary. Isolation of the acidic product *via* sodium hydrogen carbonate solution and ether gave a solid which was extracted with boiling light petroleum (b. p. 60—80°); the *half-ester* (0·42 g.) separated from the petroleum on cooling; it had m. p. 134—135° (Found: C, 59·4, 59·8; H, 4·0, 3·5. $C_9H_8O_4$ requires C, 60·7; H, 3·4%).

(*b*) The same reactants in 5 c.c. of acetone and 50 c.c. of water were treated with hydrogen peroxide (20 c.c.; " 100-vol."), added slowly below the surface of the liquid at 0—10°, during 15 min. Isolation as above gave the half-ester (0·37 g.), m. p. and mixed m. p. 134—135°.

Treatment with diazomethane gave the corresponding diester, m. p. 74—75°, which was unexpectedly unstable and gave poor analytical data.

7-*Aminocarbonylhept*-2-*ene*-4 : 6-*diynoic Acid* (*Diatretyne*-I).—The above half-ester (200 mg.) was added to ammonia solution (*d* 0·88; 5 c.c.) at −5°. After 3 hr. the mixture was cooled to −25°, acidified cautiously with concentrated hydrochloric acid, and extracted with ethyl acetate. Removal of the solvent under reduced pressure left a solid which was extracted with boiling ether; evaporation of the extract and recrystallisation from methanol gave the *half-amide* (80 mg.), decomp. above 195° (Found: C, 58·2, 58·3; H, 3·55, 3·75; N, 8·4. $C_9H_5O_3N$ requires C, 58·9; H, 3·1; N, 8·6%). Light absorption: max. 2230, 2600, 2750, 2900, and 3090 Å (ε 38,000, 12,000, 17,000, 23,000, and 18,500, respectively). A sample of natural origin showed absorption maxima which were identical, within experimental error; Anchel [1] gives 2250, 2600, 2750, 2910 and 3100 Å. Infrared spectra of Nujol suspensions were sufficiently detailed and were identical. On hydrogenation over platinic oxide in ethanol (uptake 92% of the calculated volume), suberamic acid, m. p. 144—145°, was formed quantitatively (Anchel [1] gives m. p. 144—145°).

### *Diatretyne*-II

7-*Cyanohept*-2-*ene*-4 : 6-*diyn*-1-*ol*.—Cuprous chloride (240 g.) was dissolved in 10% ammonia solution (200 c.c.) under nitrogen, and ammonium chloride (320 g.) and water (2·5 l.) were added.

[17] Bu'Lock, Jones, Leeming, and Thompson, *J.*, 1956, 3767.
[18] Cook, Jones, and Whiting, *J.*, 1952, 2883.
[19] Heilbron, Jones, and Sondheimer, *J.*, 1947, 1586.

XUM

A mixture of pent-2-en-4-yn-1-ol (29 g.) and propiolonitrile (6·0 g.) was run in with stirring, and after 5 min. the yellow precipitate was collected and washed with water until the washings became almost colourless. The wet precipitate was suspended in water (500 c.c.) and stirred briskly while a solution of potassium ferricyanide (320 g.) in water (1 l.) was added during 40 min., the colour changing to dark brown. Ether (300 c.c.) was added, and the stirring was continued for 10 min. The resulting emulsion was centrifuged for 5 min. at 20,000 r.p.m., the ethereal phase was separated, and the aqueous phase and precipitate were stirred with a similar quantity of ether, again separated by centrifugation. After drying ($MgSO_4$), the ether was distilled off and the residual solid (14 g.) was repeatedly extracted with boiling light petroleum (b. p. 60—80°; 250 c.c. in all). Evaporation gave a solid (3·5 g.) which was crystallised from carbon disulphide, giving the *alcohol* (2·1 g.), m. p. 95—101°, raised by sublimation to 100—101°, with preliminary sintering (Found: C, 72·55; H, 3·9; N, 10·4. $C_9H_5ON$ requires C, 73·25; H, 3·85; N, 10·65%). Deca-2 : 8-diene-4 : 6-diyne-1 : 10-diol was recovered in quantity from the petrol-insoluble residue.

7-*Cyanohept-2-ene*-4 : 6-*diynoic Acid* ("*Diatretyne* II").—The above alcohol (0·5 g.) in acetone (5 c.c.) was treated with a solution of chromic acid (2M in 6M-sulphuric acid; 2·8 c.c.) during 5 min. with external cooling to *ca.* −15°. After a further 40 min. the mixture was rendered homogeneous by addition of ice-water and extracted with ether (3 × 30 c.c.). Isolation of the acidic fraction and removal of the solvent under reduced pressure gave the crude acid (300 mg., 50%), m. p. 170—179°. Crystallisation from ether–light petroleum at −70° gave *diatretyne*-II as short needles, m. p. 179—180° (decomp.) (Found: C, 66·2; H, 2·05; N, 9·65. $C_9H_3O_2N$ requires C, 65·95; H, 2·0; N, 9·5%).

*Methyl* 7-*Cyanohept-2-ene*-4 : 6-*diynoate* (with J. S. Stephenson).—(*a*) The foregoing acid (220 mg.) was treated with 3% sulphuric acid in methanol at 20° for 48 hr. Isolation of the neutral fraction with ether gave the *ester* (230 mg.) as needles, m. p. 102—103·5° (from methylene dichloride–hexane) (Found: C, 68·3; H, 3·0; N, 8·8. $C_9H_5O_2N$ requires C, 67·9; H, 3·15; N, 8·8%). Light absorption: max. 2315, 2410, 2530, 2685, 2840, 3020, and 3220 Å ($10^{-3}\varepsilon$ 42·5, 63, 4·6, 9·1, 18·5, 26·5, and 19·6, respectively).

(*b*) A sample of nudic acid B (see footnote, p. 951), which had been stored for 10 years at room temperature and had become black (10·5 mg.), was similarly treated with methanolic sulphuric acid. The ester (5 mg.) had m. p. 100—104°, undepressed on admixture with the synthetic sample, and showed identical ultraviolet and infrared absorption spectra (in $CCl_4$).

### *Agrocybin*

*Methyl* 8-*Hydroxyocta*-2 : 4 : 6-*triynoate*.—To a solution of cuprous chloride (10 g.) and ammonium chloride (16 g.) in water (50 c.c.), penta-2 : 4-diyn-1-ol [9] (2 g.) and methyl propiolate (2·1 g.) in ethanol (6 c.c.) were added. The mixture was cooled in ice and salt, and 30% hydrogen peroxide (20 c.c.) was added during 1 hr., the temperature remaining below 4°. The mixture was acidified with hydrochloric acid and extracted with ether. The solvent was evaporated, and the residue was chromatographed on deactivated alumina. Evaporation of the benzene eluate gave a residue which solidified and was crystallised four times from methylene chloride at −70°, giving the ester, m. p. 38·5—41·5°. Its structure was confirmed by the spectrographic data above, but it could not be analysed because of the acquisition of static electric charge when disturbed.

8-*Hydroxyocta*-2 : 4 : 6-*triynamide* (*Agrocybin*).—The above ester (110 mg.) was treated with ammonia solution (*d* 0·88; 2 c.c.) at −5° for 7 min. The solution was then brought to room temperature and extracted with ethyl acetate (40 c.c. in all). After being washed with N-sulphuric acid and dried ($MgSO_4$), the extract was evaporated at 20°. The residue crystallised from tetrahydrofuran–methylene chloride, giving the *amide* (40 mg.) (Found: C, 64·9; H, 3·8; N, 10·8. $C_9H_6O_2N$ requires C, 65·3; H, 3·4; N, 9·5%).

Part of this work was made possible by a Maintenance Grant by the Department of Scientific and Industrial Research (to G. H. M.). We are much indebted to Dr. M. Anchel for information before its publication and for helpful discussions. Microanalyses were by Mr. E. S. Morton and his assistants, and for spectrographic determinations we are indebted to Miss W. Peadon and Mrs. J. Hopkins, working under the direction of Dr. G. D. Meakins.

The University, Manchester 13.
The Dyson Perrins Laboratory, Oxford University. [*Received, October 8th*, 1957.]

## 192. *The Infrared Spectrum of Thioformamide.*

By Mansel Davies and W. Jeremy Jones.

The spectrum of thioformamide has been studied from 400 to 5000 cm.$^{-1}$. No indications of any form other than that of the amide structure, H·C(:S)·$NH_2$, were detected, although there is strong hydrogen-bond association in the liquid state. The assignment of the twelve fundamental frequencies is considered and, in relation to the recognition of a ν(C=S) mode, the limitations of the concept of "characteristic bond frequencies" are emphasised.

There has been frequent and detailed discussion of the vibrational spectra of the amides, but far fewer accounts of the thioamide spectra are available and there is uncertainty as to the assignment of what might be expected as the characteristic frequencies of the S=C–N group. Accordingly we have studied thioformamide, the first member of the series R·C(:S)·$NH_2$, although it will not necessarily be typical of the group. No systematic account of its infrared or Raman spectrum appears to have been published.

### Experimental

Thioformamide, prepared by Gabriel's method [1] and purified as by Willstätter and Wirth,[2] had m. p. 28—29° (lit., 29°). The solid shows obvious signs of decomposition if kept at room temperatures for about ½ hr.; in diethyl ether solution it may be kept for much longer (preferably below room temperature) without decomposition. It is only sparingly soluble in solvents suitable for determination of infrared spectra, but by means of a double-beam spectrometer numerous features of the spectra from 2 to 15 μ were recorded in a 0·11 mm. cell for MeCN solutions and in a 2·5 mm. cell for $CCl_4$ solutions; for the latter solvent cells up to 4 cm. thickness could be used in the 3 μ region.

Liquid films were examined from 2 to 25 μ. They were prepared as follows: (i) by evaporation of an ethereal solution on a rock-salt plate, producing a solid film which, when covered with a second plate and placed in the radiation beam, became a liquid film; (ii) a little solid thioformamide precipitated from ethereal solution by light petroleum was placed between rock-salt plates and melted by warming. The spectra thus obtained were identical and no features ascribable to hydrogen sulphide formed on decomposition could be detected in the records. From 2 to 15 μ spectra were obtained on a Grubb-Parsons double-beam grating spectrometer (G.S.2) and from 15 to 25 μ on a Grubb-Parsons single-beam (S.3) instrument with a potassium bromide prism.

### Results and Discussion

Analogously to the position with amides, a tautomeric imino-form, HS·CH:NH, has on occasions been suggested for thioformamide. In the spectra we failed to detect any trace of a ν(SH) absorption or of any other features suggesting the presence of a tautomer. Accordingly, assuming the amino-form of the molecule, we can describe the twelve fundamental vibrational modes in the following approximate terms: $\nu_a(NH_2)$: $\nu_s(NH_2)$: the in-plane bending mode $\delta(NH_2)$: ν(C–H): the two deformation modes δ(CH) and γ(CH) respectively within and perpendicular to the (NCS) plane: $\nu_a$(NCS): $\nu_s$(NCS): δ(NCS): and, on the assumption of an all-planar form of the molecule, an in-plane rocking motion of the ($NH_2$) group, $\tau(NH_2)$: the in-phase out-of-plane motion of the two hydrogen atoms which may be designated wagging ($NH_2$): and the out-of-phase version of the same displacements which is a twisting ($NH_2$). The wave numbers of the absorptions observed together with estimated relative intensities are given in Table 1.

Apart from features arising from associated molecules, the $CCl_4$ solutions show in the 3 μ region three major absorption centres, at 3495, 3374, and 2965 cm.$^{-1}$. These are respectively, $\nu_a(NH_2)$, $\nu_s(NH_2)$, and ν(CH) in the monomeric molecules. On association

[1] Gabriel, *Ber.*, 1916, **49**, 1115.
[2] Willstätter and Wirth, *Ber.*, 1909, **42**, 1908.

further frequencies appear for the ($NH_2$) modes, at **3461** and **3174** cm.$^{-1}$ in $CCl_4$ and also at **3276** cm.$^{-1}$ in the liquid. In similar media the mean value $\frac{1}{2}(\nu_a + \nu_s)$ for the ($NH_2$) stretching modes is **3464** cm.$^{-1}$ for formamide[3] and **3383** cm.$^{-1}$ for methylamine.[4] In the gaseous state the former is all-planar whilst the methylamine almost certainly has pyramidally directed ($\sim sp^3$) nitrogen valencies. The mean value for thioformamide

TABLE 1. *Thioformamide: infrared absorptions (cm$^{-1}$).*

| Liquid | $CCl_4$ soln. | MeCN soln. | Assignment |
|---|---|---|---|
| — | 3790(<1) | — | — |
| — | 3685(1) | 3657(<1) | — |
| — | — | 3540(1) | — |
| 3481(6) | 3495(9) | 3406(9) | $\nu_a(NH_2)$ |
| — | 3461(sh) | — | — |
| 3320(9) | 3374(10) | 3312(10) | $\nu_s(NH_2)$ |
| 3276(10) | — | 3209(9) | $\nu(NH_2)$ associated |
| 3160(10) | 3174(3) | 3165(7) | $\nu(NH_2)$ associated |
| 2990(6) | 2965(3) | 2965(4) | $\nu$(CH) |
| — | 2924(<1) | — | 1599 + 1308(?) |
| 2747(3) | 2716(1) | 2748(1) | 1615 + 1123 = 2738 |
| | | | 1443 + 1288 = 2731 |
| 2455(2) | 2459(1) | 2476(<1) | 1615 + 842 = 2457 |
| 2272(1) | — | — | 1443 + 842 = 2285 |
| | | | 1615 + 673 = 2288 |
| — | 1720(1) | 1699(2) | 2 × 863 = 1726 |
| 1657(3) | 1658(<1) | — | 2 × 842 (liq.) = 1684 |
| | | | 3276 − 1615 = 1661 |
| 1615(6) | 1599(2) | 1603(7) | $\delta(NH_2)$ |
| 1472(1) | — | 1477(1) | 842 + 626 = 1468 |
| 1457(2) | 1457(1) | 1457(1) | — |
| 1443(7) | 1432(10) | 1426(4) | $\nu_a$(NCS) |
| 1324(5) | 1308(5) | 1315(5) | $\delta$(CH) |
| 1288(3) | 1287(5) | 1289(7) | $\nu_s$(NCS) |
| 1123(5) | 1125(3) | 1129(7) | rock ($NH_2$) |
| 984(5) | 942(2) | 982(5) | $\gamma$(CH) |
| 824(6) | 863(2) | 858(8) | $w(NH_2)$ |
| 673 (broad) | — | 671 (broad) | $t(NH_2)$ |
| 626 (broad) | — | — | $\delta$(NCS) |

(**3435** cm.$^{-1}$) lies between the above extremes and may, perhaps, be taken to suggest that thioformamide too tends to assume a planar configuration of its nitrogen valencies. The intensity and the appreciable lowering in frequency shown by the $\nu(NH_2)_{associated}$ modes emphasise the extent and the strength of the hydrogen-bonding in the liquid state.

The location of $\nu$(CH) in thioformamide at **2965** cm.$^{-1}$ compares with values of **2930** cm.$^{-1}$ for formic acid [5] and **2860** cm.$^{-1}$ for formamide (all in $CCl_4$).

The medium intensity absorption showing the displacements (in cm.$^{-1}$), **1599** ($CCl_4$) ⟶ **1603** (MeCN) ⟶ **1615** (liquid), conforms to the location and behaviour expected for the $\delta(NH_2)$ mode.

The remaining well-defined absorptions for the liquid in the rock-salt region (and their relative intensities) are: **1443** (7), **1324** (5), **1288** (3), **1123** (5), **984** (5), **842** (6) cm.$^{-1}$. In vinyl compounds (*i.e.*, $CH_2$=CHX) a characteristic band near **990** cm.$^{-1}$ arises from the out-of-plane $\gamma$(CH) mode: somewhat higher values are found in typical formate derivatives [3, 5, 6] (Table 2), but there is little doubt that the **984** cm.$^{-1}$ feature in thioformamide is the $\gamma$(CH) absorption. Substituted ethylenes give the range **1300**—**1400** cm.$^{-1}$ as containing the $\delta$(CH) mode and further comparison with Table 2 leads to the choice of **1324** cm.$^{-1}$ for this absorption in thioformamide.

It is thus entirely reasonable that the highest and most intense of the frequencies listed above should be taken as $\nu_a$(NCS), *i.e.*, **1443** cm.$^{-1}$. Randall *et al.*[7] in a set of eighteen

[3] Evans, *J. Chem. Phys.*, 1954, **22**, 1228.
[4] A. E. Parsons, this Laboratory.
[5] Thomas, *Discuss. Faraday Soc.*, 1950, **9**, 339.
[6] R. L. Jones, Ph.D. Thesis, Univ. Wales, 1955.
[7] Randall, Fowler, Fuson, and Dangl, "Infra-red Determination of Organic Structures," Van Nostrand, New York, 1949.

compounds containing the grouping (R·N=C=S) have found a strong band between 1471 and 1613 cm.$^{-1}$ which they assign to a NCS stretching mode, and more specifically they describe it as ν(C–N). There remains for the fundamental $\nu_s$(NCS) a possible choice between 1288 cm.$^{-1}$ and 1123 cm.$^{-1}$. It is to be expected that this absorption would be

TABLE 2. *Deformation* (CH) *wave numbers in formate derivatives.*

| | $H{\cdot}CO_2H$ | $H{\cdot}CO_2^-$ | $H{\cdot}CO{\cdot}NH_2$ | H·CO·NHMe |
|---|---|---|---|---|
| δ(CH) ..... | 1374 | 1365 | 1391 | 1389 |
| γ(CH) ..... | 1064 | 1069 | 1050 | 1010 |

appreciably less intense than $\nu_a$(NCS). Some support for the choice of 1288 cm.$^{-1}$ for this mode comes from a comparison with formamide [3] where the corresponding $\nu_s$(NCO) mode is at 1309 cm.$^{-1}$ and where the rocking ($NH_2$) vibration is at 1190 cm.$^{-1}$, which makes its identification with 1123 cm.$^{-1}$ in thioformamide plausible. Whilst it would not be out of the question to reverse the above assignments of $\nu_s$(NCS) and $r$($NH_2$) in thioformamide, the choice made seems the more likely one.

There is little guidance as to appropriate values for the $w$($NH_2$) and $t$($NH_2$) modes, but these could perhaps give rise to the absorptions at 842 and 673 cm.$^{-1}$. By comparison with thiourea [8] where the corresponding vibration is at 629 cm.$^{-1}$, it is not unreasonable to suggest that δ(NCS) may be at 626 cm.$^{-1}$ in thioformamide.

A question of general interest is whether in the spectrum of thioformamide we can recognise a ν(C=S) frequency. Colthup [9] has suggested the range 1300—1400 cm.$^{-1}$ for this vibration but he does not indicate the class of compounds on which the assignment is based. Sheppard [10] on the other hand has examined a number of compounds with this link and has found no clear correlation: Bellamy [11] also studied a limited number of C=S compounds and was unable to identify any bands in the 1300—1400 cm.$^{-1}$ region which could be assigned to ν(C=S). Mecke and Spiesecke [12] have assigned the frequency at 1216 cm.$^{-1}$ in dithioformic acid and that at 1302 cm.$^{-1}$ in thioacetamide to this mode. More recently Mecke, Mecke, and Lüttringhaus [13] have assigned a frequency varying from 1047 to 1208 cm.$^{-1}$ to ν(C=S) in a number of cyclic and open-chain structures. The variation in this frequency at least emphasises the dependence, if not the " mixing ", of this vibration with adjacent bonds; and the shift from 1109 to 1064 cm.$^{-1}$ in the apparent ν(C=S) on deuteration of thiopyrrolidone,[14] having the grouping (–CS·NH–), provides similar evidence.

The difficulty in assigning the description ν(C=S) in many of these cases probably arises from the location of the hypothetical isolated ν(C=S) vibration (say, approximately, 1200 cm.$^{-1}$) near the frequency of the adjacent bond, *i.e.*, ν(C–O) or ν(C–N). Accordingly these frequencies become split into $\nu_a$(XCS) and $\nu_s$(XCS) modes whose separation depends upon the degree of coincidence of the component bond frequencies and upon the interactions (or delocalisation) within the XCS bonds. In such circumstances it becomes very difficult (if not arbitrary) to decide which of the two observed frequencies $\nu_a$(XCS) or $\nu_s$(XCS) has the more ν(C=S) character. This is exemplified in such structures as thiourea where Stewart [8] has placed ν(C=S) at 1413 cm.$^{-1}$: as already indicated, Randall *et al.*[7] preferred to designate the frequency in the 1471—1613 cm.$^{-1}$ range for their NCS compounds as ν(C–N). The obvious uncertainty in these cases serves to emphasise the limitations of the concept of " a characteristic bond frequency."

We conclude that thioformamide is adequately represented by the amide formula but that it is difficult to decide which of the two bonds immediately concerned is principally

[8] Stewart, *J. Chem. Phys.*, 1957, **25**, 248.
[9] Colthup, *J. Opt. Soc. Amer.*, 1950, **40**, 397.
[10] Sheppard, *Trans. Faraday Soc.*, 1950, **46**, 429.
[11] Bellamy, " The Infra-Red Spectra of Complex Molecules," Methuen, London, 1954.
[12] Mecke and Spiesecke, *Chem. Ber.*, 1956, **89**, 1110.
[13] Mecke, Mecke, and Lüttringhaus, *ibid.*, 1957, **90**, 975.
[14] Mecke and Mecke, *ibid.*, 1956, **89**, 343.

involved in the pseudo-symmetric, and which in the pseudo-antisymmetric stretching mode of the (NCS) grouping.

A grant from the Ministry of Education to one of us (W. J. J.) is gratefully acknowledged, and also the essential support given by Imperial Chemical Industries Limited, Shell Petroleum, and Unilever Ltd., in the purchase of infrared equipment.

THE EDWARD DAVIES CHEMICAL LABORATORIES,
THE UNIVERSITY COLLEGE OF WALES, ABERYSTWYTH. [*Received, October 14th*, 1957.]

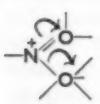
---

## 193. *Heats of Combustion and Molecular Structure. Part IV.* Aliphatic Nitroalkanes and Nitric Esters.*

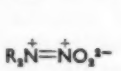
By R. C. CASS, S. E. FLETCHER, C. T. MORTIMER, P. G. QUINCEY, and H. D. SPRINGALL.

The heats of combustion of nitromethane, nitroethane, 1-nitropropane, 2-nitropropane, dimethylnitramine, and diethylnitramine have been measured. The group-energy terms for the ($C-NO_2$) and ($N-NO_2$) groups are derived from these data and that for ($O-NO_2$) from published data. The significance of the results is considered.

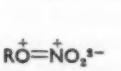
ANALYSIS of the molecular energetics (mean bond- and resonance-energy terms) for the $X-NO_2$ system, where $X = R_3C$, $R_2N$, and RO, is of general interest and particularly desirable in view of the practical importance of thermal data on such compounds. The analysis is complicated by (i) the simultaneous occurrence of formal charge and resonance effects within the grouping (I), (ii) uncertainties in the values of the mean bond-energy terms for the bonds N–O and N=O, and (iii) the probability, when $X = R_2N$ or RO, of additional mesomerism involving the excited structures (II) and (III). We have therefore approached the analysis in stages, evaluating first, from heats of combustion and latent



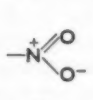
(I)



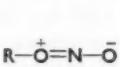
(II)



(III)



(IV)



(V)

heats, the " group-energy term " for each of the three types of $X-NO_2$ group, $E(C-NO_2)$, $E(N-NO_2)$, and $E(O-NO_2)$. The group-energy term is the enthalpy change, $-\Delta H$, for the hypothetical gas-phase formation of the nitro-group, *e.g.*, $E(C-NO_2)$ is $-\Delta H$ for $R_3C\cdot + N + 2O \longrightarrow R_3C-NO_2$, *i.e.*, the group energy is that part of the atomic heat of formation, $-\Delta H_{f,a}$, of the nitro-compound corresponding to the actual formation and attachment of the nitro-group, and includes formal charge and resonance effects, mean bond-energy terms, and any additional mesomeric effects. These group-energy terms can be used directly in the evaluation of $-\Delta H_{f,a}$ terms for hypothetical nitro-compounds of all three classes.

We have attempted to carry the analysis a stage further and to disentangle the various components of the group-energy terms.

### EXPERIMENTAL

*Materials.—Benzoic acid.* The B.D.H. thermochemical standard product ($-\Delta U_b = 6{\cdot}3181 \pm 0{\cdot}0007$ kcal./g.†) was used.

*Nitroalkanes.* These (I.C.I.) were each distilled through an 18 in. column packed with glass helices. Fractions collected were: nitromethane, b. p. 99·7—99·9°/750 mm. (lit.,[1]

* Parts I—III, *Trans. Faraday Soc.*, 1954, **50**, 815; *J.*, 1954, 2764; 1955, 1188.

† 1 Thermochemical calorie = 4·1840 abs. Joules.

[1] Heilbron and Bunbury, " Dictionary of Organic Compounds," London, 1946.

100·8°/760 mm.); nitroethane, b. p. 114·0—114·1°/750 mm. (lit.,[1] 114—114·8°/760 mm.); 1-nitropropane, b. p. 128·2—128·4°/732 mm. (lit.,[1] 130·5—131·5°/760 mm.); 2-nitropropane, b. p. 120·0—121·0°/760 mm. (lit.,[1] 120°/760 mm.).

*Nitramines.* Dimethyl- and diethyl-nitramine were prepared by dehydration of dimethyl- and diethyl-ammonium nitrate, respectively.[2] *NN*-Dimethylacetamide, formed as an impurity in this preparation of diethylnitramine, was removed by 3 hours' refluxing with 85% w/w sulphuric acid.[3] The nitramines were distilled through an 8 in. column packed with Fenske helices. Fractions collected were: dimethylnitramine, b. p. 64·0—64·4°/9 mm. (Chute, Herring, Toombs, and Wright give 70°/25 mm.); diethylnitramine, 53·2°/2 mm. (Backer [4] gives 93°/16 mm. and 206·5°/757 mm.). The dimethylnitramine, five times recrystallised from ether, had m. p. 55·0—55·3° (Chute *et al.*[2] give 57°). Dimethylnitramine was also prepared by the nitrolysis of *as.*-dimethylurea.[5] This specimen, recrystallised five times from light petroleum, had m. p. 55·0—55·2°.

*Combustion Calorimetry.*—The nitroalkanes were burnt in the stainless steel, single valve, Mahler–Cook bomb of energy equivalent, $E$, 31,199 ± 8·0 cal./ohm, by the procedure described in Part III. Results are shown in Table 1.

TABLE 1.

| $m_{(vac)}$ (g.) | $\Delta R$ (ohm) | Corrections (cal.) Fuse | $HNO_3$ | Carbon | $C$ (cal./ohm) | $-\Delta U_b$ * (kcal./mole) |
|---|---|---|---|---|---|---|
| | | Nitromethane, $M$ = 61·04 | | | | |
| 2·4646 | 0·22566 | 83·7 | 22·0 | 0·4 | 10·1 | 174·5 |
| 1·9613 | 0·18376 | 93·1 | 20·9 | 0·5 | 8·0 | 175·1 |
| 1·7572 | 0·16418 | 90·6 | 19·5 | 0·5 | 7·2 | 174·5 |
| | | Nitroethane, $M$ = 75·07 | | | | |
| 1·5337 | 0·21762 | 94·1 | 20·7 | 2·4 | 10·3 | 326·8 |
| 1·4283 | 0·20191 | 80·6 | 13·4 | 0 | 9·6 | 326·9 |
| 1·3195 | 0·18743 | 99·2 | 17·4 | 7·1 | 8·9 | 326·5 |
| | | 1-Nitropropane, $M$ = 89·09 | | | | |
| 1·4531 | 0·25280 | 107·8 | 25·5 | 1·96 | 11·1 | 481·7 |
| 0·9880 | 0·17377 | 96·4 | 11·1 | 2·35 | 7·6 | 479·4 |
| 1·0032 | 0·17755 | 102·5 | 13·7 | 1·96 | 7·6 | 481·8 |
| 1·0160 | 0·17760 | 105·4 | 13·3 | 1·96 | 7·8 | 482·1 |
| 1·0630 | 0·18759 | 69·2 | 14·8 | 0 | 8·1 | 483·4 |
| | | 2-Nitropropane, $M$ = 89·09 | | | | |
| 1·2529 | 0·21487 | 98·5 | 19·2 | 0·7 | 9·6 | 477·8 |
| 1·1645 | 0·20402 | 108·6 | 14·4 | 0·5 | 8·9 | 478·5 |
| 0·9318 | 0·16244 | 77·1 | 7·3 | 2·0 | 2·0 | 477·6 |
| 0·8627 | 0·15102 | 87·9 | 12·2 | 3·9 | 6·6 | 477·5 |

* Where $-\Delta U_b = 10^{-3}M/m$ [$(E + C)\Delta R$ − corrections for fuse + nitric acid + carbon].

The nitramines were burnt in a twin-valve bomb (the Parr Instrument Company, Moline, Illinois, U.S.A.), made of Carpenter 20 alloy and having an internal volume of 340 ml. The inlet and outlet valves are seated in Kel-F plastic. The sample to be burnt was placed in a flat platinum crucible, supported by a platinum ring attached to the inlet tube. The energy equivalent, $E$, of the calorimeter system containing this Parr bomb was determined, by burning benzoic acid pellets, as 39,980·0 ± 24·0 cal./ohm.

The twin-valve arrangement allows the gaseous products of combustion to be swept out of the bomb and analysed. The amount of carbon dioxide present in the bomb gases after combustion was estimated in an analysis train similar to that described by Prosen and Rossini.[6] The following figures are typical for the quotient of (observed)/(calculated) $CO_2$ in calibration experiments: 1·0007, 0·9993, 1·0001, 1·0000. When dimethylnitramine was burnt there was produced 99·1—99·6% of the calculated quantity of carbon dioxide. As no carbon was evident and a slight smell of nitramine remained, the heat of combustion was calculated by assuming that the carbon dioxide produced represented the nitramine burnt.

When burning the liquid diethylnitramine, a small amount of petroleum jelly was used with

[1] Chute, Herring, Toombs, and Wright, *Canad. J. Research*, 1948, **26**, *B*, 95 and 129.
[2] Lamberton, personal communication.
[3] Backer, *Sammlung Chem. Vorträge*, 1912, **18**, 359.
[4] Franchimont, *Rec. Trav. chim.*, 1896, **15**, 211.
[5] Prosen and Rossini, *J. Res. Nat. Bur. Stand.*, 1941, **27**, 289.

the filter paper fuse. The heat of combustion of the petroleum jelly was taken as 11·4 kcal./g. from controls.

Diethylnitramine burnt violently, and in two combustions the Neoprene sealing ring in the head of the bomb was burnt. This was avoided by inserting a platinum crucible about 2 cm. above the sample, as a baffle. Combustion was then incomplete to the extent of about 1%, and carbon was deposited; corrections were made by taking the heat of combustion of carbon as 7·838 kcal./g. Results are given in Table 2.

TABLE 2.

| $m_{(vac.)}$ (g.) | Obs./Calc. $CO_2$ | $\Delta R$ (ohm) | Corrections (cal.): Fuse paper | Fuse jelly | $HNO_3$ | Incomplete combustion | $C$ (cal./ohm) | $-\Delta U_b$ * (kcal./mole) |
|---|---|---|---|---|---|---|---|---|
| Dimethylnitramine, $M$ = 90·10 | | | | | | | | |
| 1·8658 | 0·9941 | 0·19459 | 6·0 | — | 34·4 | 45·9 | 12·6 | 377·4 |
| 1·8109 | 0·9909 | 0·18898 | 6·0 | — | 33·6 | 68·8 | 12·2 | 376·0 |
| 1·7558 | 0·9948 | 0·18343 | 6·0 | — | 36·4 | 38·1 | 11·8 | 376·1 |
| 1·8089 | 0·9958 | 0·18928 | 6·0 | — | 34·9 | 31·8 | 12·2 | 376·5 |
| Diethylnitramine, $M$ = 118·14 | | | | | | | | |
| 0·3415 | 0·9941 | 0·05116 | 6·4 | 38·8 | 5·3 | 6·4 | 1·0 | 692·3 |
| 0·4121 | 0·9867 | 0·06118 | 6·0 | 25·1 | 4·3 | 17·6 | 1·0 | 695·6 |
| 0·5822 | 0·9990 | 0·08091 | 12·4 | 35·3 | 12·2 | 1·7 | 1·0 | 694·1 |

* Where $-\Delta U_b = 10^{-3}M/m$ [$(E + C)\Delta R$ − corrections for fuse paper + fuse jelly + nitric acid − incomplete combustion].

The $-\Delta U_b$ terms were converted into $-\Delta H_c^\circ$ terms, the standard heat of combustion (Table 3), through the expression

$$-\Delta H_c^\circ = -\Delta U_b - w - \Delta nRT$$

where $w$ is the Washburn correction, calculated according to Prosen,[7] and $\Delta n$ is the number of molecules of gas produced in the combustion of one molecule of the substance.

Independent $-\Delta H_c^\circ$ data on the nitroalkanes were (*a*) published (Holcomb and Dorsey [8]) during the preliminary stages of our study, and (*b*) made available recently in personal communication from the National Bureau of Standards, Washington. These data are listed for

TABLE 3.

| | Nitro-methane | Nitro-ethane | 1-Nitro-propane | 2-Nitro-propane | Dimethyl-nitramine | Diethyl-nitramine |
|---|---|---|---|---|---|---|
| Mean $-\Delta U_b$ (kcal./mole) | 174·4 | 326·7 | 481·7 | 477·8 | 376·5 | 692·4 |
| Deviation (%) | 0·17 | 0·10 | 0·14 | 0·06— | 0·10 | 0·15 |
| Washburn correction, $w$ (kcal./mole) | 0·20 | 0·22 | 0·26 | 0·26 | 0·08 | 0·35 |
| $\Delta nRT$ (kcal./mole) | +0·15 | −0·15 | −0·45 | −0·45 | +0·30 | −0·30 |
| $-\Delta H_c^\circ$ (kcal./mole): | | | | | | |
| This work | 174·4 ± 0·3 | 326·6 ± 0·3 | 481·8 ± 0·7 | 478·0 ± 0·3 | 376·1 ± 1·0 | 692·4 ± 2·0 |
| Holcomb and Dorsey | 175·25 ± 0·18 | 325·42 ± 0·3 | 481·22 ± 0·61 | 477·43 ± 0·17 | — | — |
| N.B.S. | 169·49 ± 0·14 | 324·57 ± 0·25 | 480·91 ± 0·29 | 478·17 ± 0·19 | — | — |
| $-\Delta H_f^\circ$ (kcal./mole) | 22·2 ± 0·3 | 32·3 ± 0·3 | 39·5 ± 0·7 | 43·2 ± 0·3 | 17·0 ± 1·0 | 25·3 ± 2·0 |
| $L_g^{298}$ (kcal./mole) | 9·1 ± 0·1 [a] | 9·4 ± 0·1 [a] | 10·4 ± 0·1 [a] | 9·9 ± 0·1 [a] | 16·7 [b] | 11·5 [a] |

[a] Calc. from measurements made by Mr. B. Sutcliffe of the variation of vapour pressure with temperature over the range 65—105°, when $\log_{10} p = 8{\cdot}302 - 2595/T$, where $p$ is in mm. Hg and $T$ in °K.

[b] Hodge, *Ind. Eng. Chem.*, 1940, **32**, 748. [b] Bradley, Cotson, and Cox, *J.*, 1952, 740.

comparison in Table 3. Our $-\Delta H_c^\circ$ values for the nitroalkanes correspond well with those from both other sources except for nitromethane, where the Bureau value for $-\Delta H_c^\circ$, 169·5 kcal./mole, is significantly lower than ours and is in accord with the value 169·4 kcal./mole

[7] Prosen, "Experimental Thermochemistry," ed. Rossini, Interscience, New York, 1956.
[8] Holcomb and Dorsey, *Ind. Eng. Chem.*, 1949, **41**, 2788.

derived by Bichowsky and Rossini [9] from earlier studies. Our $-\Delta H_c^\circ$ for diethylnitramine is close to the value 69·2 ± 0·9 kcal./mole quoted by Laidler.[10]

Also listed in Table 3 are the terms $-\Delta H_f^\circ$ (heat of formation of the compound in its standard state from the elements in their standard states, calculated from $-\Delta H_c^\circ$ by assuming the $-\Delta H_f^\circ$ terms: $H_2O$, 68·3174; $CO_2$, 94·0518 kcal./mole [11]), $L_g^{st}$ ($\Delta H$ for the change of the compound in the standard state to the gaseous compound), and the derived $-\Delta H_{f,g}^{st}$ (heat of formation of the gaseous compound from the elements in their standard states).

## Discussion

The atomic heats of formation, $-\Delta H_{f,a}$ (Table 4), were calculated from the $-\Delta H_{f,g}^{st}$ terms (Table 3) and the heats of atomisation, $\Delta H_a$, of the elements: C, 171·7; [12] H, 52·09; [11] O, 58·98; [13] N, 113·0 [14] kcal./g.-atom.

Group-energy terms are most simply evaluated from $\bar{E}(X\text{–}NO_2) = -\Delta H_{f,a} - \sum'\bar{E}(b)$, in which expression $\sum'\bar{E}(b)$ is the sum of the mean bond-energy terms for all the bonds in the molecule other than those in the $X\text{–}NO_2$ system. However, $\bar{E}$(C–H) is in fact not quite constant among the lower paraffins [15] and use of a constant value for this expression would introduce errors into the evaluation of $\bar{E}(X\text{–}NO_2)$. We therefore evaluate $\bar{E}(X\text{–}NO_2)$ (Table 4) by considering the hypothetical substitution $R_nX\text{–}H + N + 2O \longrightarrow R_nX\text{–}NO_2 + H$, from which $\bar{E}(X\text{–}NO_2) = -\Delta H_{f,a}(R_nX\text{–}NO_2) + \Delta H_{f,a}(R_nX\text{–}H) - \bar{E}(X\text{–}H)$, and use, instead of the general $\bar{E}$(C–H) = 98·85 kcal./mole, the particular values of $\bar{E}$(C–H) derived from the appropriate hydrocarbons by using $\bar{E}$(C–C) = 83·1 kcal./mole,[16] together with those for $\bar{E}$(N–H) and $\bar{E}$(O–H) derived from the appropriate amines and alcohols [16] (Table 4). The $-\Delta H_{f,a}(R_nX\text{–}H)$ terms (Table 4) are derived from the $-\Delta H_{f,g}^{st}$ terms: hydrocarbons: [17] methane; 17·89; ethane, 20·24; propane, 24·82: secondary amines: [18] dimethyl-, 6·6; diethyl-, 20·3: alcohols: methyl,[11] 48·08; ethyl,[11] 56·24; *n*-propyl,[19] 63·64 kcal./mole. The $-\Delta H_{f,a}(RO\text{–}NO_2)$ terms (Table 4) are derived from the corresponding $-\Delta H_{f,g}^{st}$ terms for the nitrate esters: [20] methyl, 29·0; ethyl, 37·0; *n*-propyl, 43·9 kcal./mole.

Table 4. $-\Delta H$ *data for* $R_nX$ (*kcal./mole*).

| | Me | Et | Pr$^n$ | Pr$^i$ | $Me_2N$ | $Et_2N$ | MeO | EtO | Pr$^n$O |
|---|---|---|---|---|---|---|---|---|---|
| $-\Delta H_{f,a}$ ($R_nX\text{–}NO_2$) ..... | 572·2 | 857·7 | 1139·8 | 1144·0 | 1000·2 | 1565·5 | 646·9 | 930·8 | 1213·6 |
| $-\Delta H_{f,a}$ ($R_nX\text{–}H$) ..... | 397·9 | 676·1 | 956·6 | 956·6 | 827·6 | 1393·1 | 487·1 | 771·1 | 1054·4 |
| $\bar{E}(X\text{–}H)$ ..... | 99·5 | 99·2 | 98·7 | 98·7 | 93·0 | 93·0 | 110·0 | 110·0 | 110·0 |
| $\bar{E}(X\text{–}NO_2)$ ..... | 273·6 | 280·8 | 281·9 | 286·1 | 265·4 | 265·4 | 269·8 | 269·7 | 269·2 |

$\bar{E}(C\text{–}NO_2)$ *Terms from Nitroalkanes.*—The values from nitroethane and the nitropropanes are reasonably concordant, the mean being 282·9 kcal./mole. The value from our (and Holcomb and Dorsey's) nitromethane combustion data, 273·6 kcal./mole, is much lower. $\bar{E}(C\text{–}NO_2)$ derived from the nitromethane data from the National Bureau of

[9] Bichowsky and Rossini, "The Thermochemistry of the Chemical Substances," Reinhold, New York, 1936.
[10] Laidler, *Canad. J. Chem.*, 1956, **34**, 626.
[11] National Bureau of Standards, Circular 500, Washington, 1952.
[12] Brewer and Kane, *J. Phys. Chem.*, 1955, **59**, 105.
[13] Brix and Herzberg, *J. Chem. Phys.*, 1953, **21**, 2240.
[14] Frost and McDowell, *Proc. Roy. Soc.*, 1956, *A*, **236**, 278.
[15] Prosen and Rossini, *J. Res. Nat. Bur. Stand.*, 1945, **34**, 263.
[16] Coates and Sutton, *J.*, 1948, 1187.
[17] Selected Values of Properties of Hydrocarbons, American Petroleum Institute, Research Project 44, Carnegie Institute of Technology, Pittsburg, 1954.
[18] Thomsen, "Systematische durchsührung Thermochemischer Untersuchungen," Enke, Stuttgart, 1906, p. 343.
[19] Rossini, *J. Res. Nat. Bur. Stand.*, 1934, **13**, 189.
[20] Gray, XXVII Congresso Internacional de Quimica Industrial, 1954.

Standards is 279·4 kcal./mole, much closer to those from the other nitroalkanes. Pending a further study of nitromethane, we take $\overline{E}(C-NO_2) = 283$ kcal./mole for (*a*) computing the $-\Delta H_{f,a}$ terms for hypothetical nitroalkanes, and (*b*) considering the energetics of this grouping.

For the approach to the analysis, to the nearest kcal., of the $\overline{E}(C-NO_2)$ group-energy term, we take $\overline{E}(C-N) = 73$ kcal./mole.[16] This yields 210 kcal./mole for the sum of the bond-energy terms and the formal charge and resonance-energy effects in the group (IV). The resonance energy of the nitro-group is probably *ca.* 25 kcal./mole.[21] A somewhat uncertain value for $\overline{E}(N-O)$, 46 kcal./mole, is available from data on hydroxylamine.[22] Satisfactory data are not available for $\overline{E}(N=O)$, since derivations from results for nitrite esters,[23] R–O–N=O, perforce neglect the effect of resonance with structure (V), etc. The value is likely to be considerably greater than twice $\overline{E}(N-O)$, 92 kcal./mole, since $\overline{E}(N=N)$, 100·3 [16] and $\overline{E}(O=O)$, 118·0 [23] are each greater than twice the corresponding single-bond-energy terms $\overline{E}(N-N)$, 39 and $\overline{E}(O-O)$, 34·9 kcal./mole.[16] We can now estimate the sum of $\overline{E}(N=O)$ and the formal charge effects in the nitro-group as $210 - (25 + 46)$, *i.e.*, 139 kcal./mole.

$\overline{E}(N-NO_2)$ *Terms from Secondary Nitramines.*—The values from dimethyl- and diethyl-nitramines are concordant. We take $\overline{E}(N-NO_2) = 265$ kcal./mole for (*a*) computing $-\Delta H_{f,a}$ terms for hypothetical nitramines and (*b*) considering the energetics of the grouping.

Since the sum of the bond-energy terms and formal charge and resonance-energy effects in the system (IV) is 210 kcal./mole, the contribution of the N–N bonding and the secondary nitramines must be 55 kcal./mole. This is 16 kcal./mole in excess of $\overline{E}(N-N)$, 39 kcal./mole, and implies a considerable contribution to the structure of the isolated molecule from the double bonded N=N structure (II). This structure infringes Pauling's "adjacent-charge rule" [21] but there are already established exceptions to this rule (*e.g.*, in the crystal structure of hydrazinium difluoride [24]). N=N Double-bonding is operative in crystalline dimethylnitramine (Costain and Cox [25]) when the $C_2N_2O_2$ system is coplanar and the N–N distance, 1·26 Å, is much shorter than the normal N–N single-bond distance [26] of 1·40 Å and is close the N=N double-bond distance,[26] 1·20 Å. Confirmation of N=N double bonding in free nitramine molecules also comes from the high dipole moment of dimethylnitramine in benzene, 4·5D.[27]

$\overline{E}(O-NO_2)$ *from Alkyl Nitrates.*—The values are closely concordant and we take $\overline{E}(O-NO_2) = 270$ kcal./mole for (*a*) computing $-\Delta H_{f,a}$ for hypothetical nitrate esters and (*b*) considering the energetics of this grouping.

Since $\overline{E}(-NO_2) = 210$ kcal./mole, the contribution of the O–N bond to $\overline{E}(O-NO_2)$ must be 60 kcal./mole. This is 14 kcal./mole in excess of $\overline{E}(O-N)$, 46 kcal. mole, and implies, analogously to the nitramines, a considerable contribution from the double bonded O=N structure (III), again infringing the adjacent-charge rule. Early electron diffraction studies of gaseous methyl nitrate [28] and an *X*-ray diffraction study of crystalline pentaerythritol tetranitrate [29] did not reveal a shortening of this O–N bond below the single-bond value,[30] 1·37 Å, but it is doubtful if the early techniques were sufficiently

[21] Pauling, "Nature of the Chemical Bond," Oxford Univ. Press, London, 1950.
[22] Bichowsky and Rossini, "The Thermochemistry of the Chemical Substances," Reinhold, New York, 1936.
[23] Cottrell, "The Strengths of Chemical Bonds," p. 253, Butterworths, London, 1954.
[24] Robertson, *Annual Reports*, 1942, **39**, 102.
[25] Costain and Cox, *Nature*, 1947, **160**, 826.
[26] Sidgwick, "Chemical Elements and their Compounds," Oxford Univ. Press, 1950, p. 709.
[27] Mortimer and Springall, unpublished observations.
[28] Pauling and Brockway, *J. Amer. Chem. Soc.*, 1937, **59**, 13.
[29] Booth and Llewellyn, *J.*, 1947, 837.
[30] Rogowski, *Ber.*, 1942, *B*, **75**, 244.

sensitive (see, *e.g.*, ref. 31) and further diffraction investigation of nitrate esters seems desirable.

We thank Imperial Chemical Industries Limited for the nitroalkanes and for a grant.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE,
KEELE, STAFFORDSHIRE. [*Received, October 14th*, 1957.]

[31] Millar, Mortimer, and Springall, *J.*, 1957, 3456.

---

## 194. *Sesquiterpenoids. Part X.* The Constitution of Lactucin.*

By D. H. R. BARTON and C. R. NARAYANAN.

Lactucin, the active principle of "lactucarium," is a sesquiterpenoid lactone giving chamazulene on dehydrogenation. On selective hydrogenation lactucin affords dihydrolactucin, then two isomeric tetrahydrolactucins, and finally the known hexahydrolactucin. On the basis of these and other changes the constitution (I; R = H) has been deduced for lactucin.

THE sesquiterpenoid lactone lactucin, $C_{15}H_{16}O_5$, is the main bitter principle of the latex of *Lactuca virosa* L. (wild lettuce). The dried latex, known in pharmacy as "lactucarium" or lettuce opium, has for long enjoyed a reputation as a hypnotic, the activity being attributed to the presence of lactucin. Chemical investigations on lactucin were initiated over a century ago,[1] but the only contributions of structural significance are those by Späth, Lorenz, and Kuhn [2] and by Wessely, Lorenz, and Kuhn.[3] The last two references cite the extensive pharmaceutical literature in detail.

Prior knowledge about the constitution of lactucin can be summarised as follows. Lactucin contains a lactone grouping, two easily esterified hydroxyl groups, and a conjugated ketonic group ($\lambda_{max.}$ 257 mμ). The molecule is sensitive to both acid and base, giving intense colour reactions. Lactucin contains one *C*-Me group and gives formaldehyde on ozonolysis. Catalytic hydrogenation affords a saturated hexahydrolactucin which gives diesters and ketone derivatives. The hexahydro-compound is stable to lead tetra-acetate, is hydrolysed by alkali to a stable hexahydrolactucinic acid, and is oxidised by potassium permanganate to methylsuccinic acid. In spite of the presence of three ethylenic linkages lactucin consumes no per-acid at 0°. Both lactucin and hexahydrolactucin gave blue oils, which were not further characterised, on dehydrogenation with selenium.

Our investigations have shown that lactucin has the constitution (I; R = H). This structure is in accord with the earlier evidence cited above and is fully justified by the following experimental facts.

Lactucin showed bands in the infrared (Nujol) at 3320 and 3240 (OH), 1755 (γ-lactone), 1662 (C=C·CO·C=C; 5-membered ring) and 1623 and 1610 (C=C conjugated with carbonyl groups) cm.$^{-1}$. The diacetate (I; R = Ac) gave maxima (in $CHCl_3$) at 1770 (γ-lactone), 1735 and 1252 (acetate), 1690 (as for 1662 above) and 1623 and 1618 (C=C, as above) cm.$^{-1}$. Hydrogenation furnished hexahydrolactucin (II; R = H), which showed infrared bands at 3340 (OH), 1775 (γ-lactone), and 1728 (*cyclo*pentanone). The hexahydro-compound readily afforded a ditoluene-*p*-sulphonate (II; R = toluene-*p*-sulphonyl), thus confirming both hydroxyl groups as easily esterified.

On complete hydrogenation over platinum in acetic acid–perchloric acid, followed by dehydrogenation with palladised charcoal, lactucin (I; R = H) gave chamazulene (III).[4] This established the carbon skeleton of lactucin as already written.

* Part IX, *J.*, 1957, 5041.

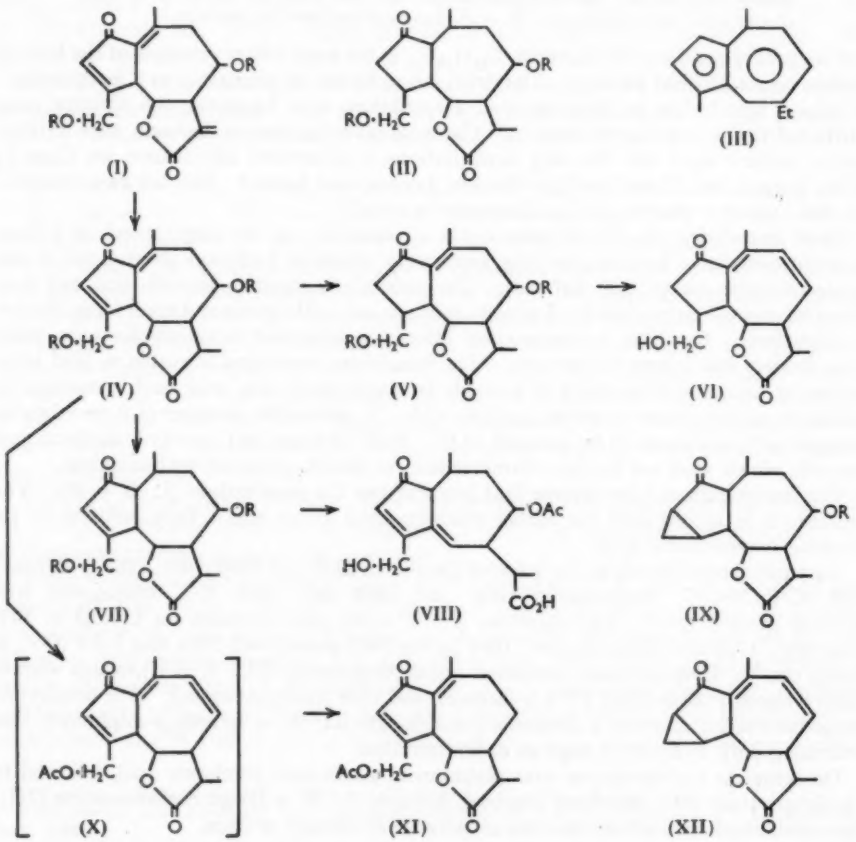
[1] Ludwig and Kromayer, *Arch. Pharm.*, 1847, **100**, 1; 1862, **161**, 1; cited by Zinke and Holzer, *Monatsh.*, 1953, **84**, 212.

[2] Späth, Lorenz, and Kuhn, *ibid.*, 1951, **82**, 114.

[3] Wessely, Lorenz, and Kuhn, *ibid.*, p. 323.

[4] Meisels and Weizmann, *J. Amer. Chem. Soc.*, 1953, **75**, 3865; Šorm, Herout, and Takeda, *Chem. Listy*, 1954, **48**, 281; Novak, Šorm, and Sicher, *ibid.*, p. 1648.

Carefully controlled catalytic hydrogenation of lactucin gave useful information on the positions of the ethylenic linkages. Absorption of one mol. of hydrogen afforded dihydrolactucin (IV; R = H), characterised as its diacetate (IV; R = Ac). Whereas lactucin gave formaldehyde on ozonolysis and contained one *C*-Me group (see above), its dihydroderivative furnished no formaldehyde and contained two *C*-Me groups. The partial hydrogenation involves, therefore, the saturation of a grouping $>C{=}CH_2$. The main chromophore of lactucin ($\lambda_{max.}$ 257 mμ) is not altered by the hydrogenation (identical absorption from 235 to 350 mμ). A subtraction curve of the spectra of lactucin and dihydrolactucin showed a maximum at 208 mμ (ε 8600). This indicates that the $>C{=}CH_2$ system must be conjugated with the lactone-carbonyl group, a conclusion which is inescapable when the siting of the ketonic group and attendant ethylenic linkages is also taken into account (see below). In the infrared spectrum dihydrolactucin showed bands (in Nujol) at 3455 and 3210 (OH), 1765 (γ-lactone), 1680 (C=C·CO·C=C; 5-membered




ring), and 1630 and 1614 (C=C, conjugated with carbonyl group) cm.$^{-1}$. The diacetate (IV; R = Ac) gave maxima (in $CHCl_3$) at 1777 (γ-lactone), 1738 and 1219 (acetate), 1690 (as above), and 1640 and 1618 (C=C, as above) cm.$^{-1}$. The spectra are thus in accord with the proposed constitutions.

Selective hydrogenation of dihydrolactucin until a further mol. of hydrogen had been

absorbed, or hydrogenation of lactucin itself to uptake of two mols., gave, after crystallisation, a sparingly soluble tetrahydrolactucin (V; R = H), characterised as its diacetate (V; R = Ac). There was no increase in *C*-Me content, but the maximum in the ultraviolet spectrum shifted to 252 mμ (ε 11,000). Further hydrogenation afforded the known hexahydrolactucin. In the infrared region tetrahydrolactucin showed maxima (in Nujol) at 3375 and 3240 (OH), 1760 (γ-lactone), 1685 (·CO·C=C; 5-membered ring), and 1600 (C=C, conjugated with carbonyl group) cm.$^{-1}$. Its diacetate gave bands (in $CHCl_3$) at 1773 (γ-lactone), 1735 and 1238 (acetate), 1710 (as for 1685 above), and 1619 (C=C, as above) cm.$^{-1}$. The intensity of the C=C band in these compounds was close to that of a ketone band. As is well known [5] this indicates a *cisoid* conformation for the enone system such as is presented in (V; R = H). Indeed lactucin and dihydrolactucin, and their respective diacetates, showed the same exaltation of the intensity of the C=C band at the *lower* wave-number.[6] The intensity of the other C=C band in these compounds was normal for a conjugated ketone.

Acetylation of the mother-liquors from the crystallisation of tetrahydrolactucin (V; R = H), followed by chromatography, gave an *iso*tetrahydrolactucin diacetate. This is formulated as (VII; R = Ac) for the following reasons. The infrared spectrum showed bands (in $CHCl_3$) at 1770 (γ-lactone), 1735 and 1238 (acetate), 1700 (·CO·C=C; 5-membered ring), and 1618 (C=C, intensity not exalted) cm.$^{-1}$. The ultraviolet absorption spectrum disclosed the band of an αβ-unsaturated ketone at 227 mμ. If one accepts (see spectral evidence above) a *cyclo*pentenone ring, then this can only have one substituent on the ethylenic linkage.[7] If the ketone group of lactucin is placed in the five-membered ring of the azulenoid skeleton, then only the chromophoric system of (I) will explain the formation of two tetrahydrolactucins with spectroscopic properties as listed above. It is of interest that the ultraviolet absorption of lactucin is not in accord with multiple maxima absorption found for comparable dienone systems contained in two six-membered rings.[8] The spectroscopic properties of such systems are clearly related to their conformations in a subtle way.[8]

Treatment of tetrahydrolactucin with alkali at room temperature gave, without acidification and, therefore, without opening of the lactone ring, a nicely crystalline dienone (VI) having an ultraviolet absorption maximum at 301 mμ. Its infrared spectrum (in $CHCl_3$) showed bands at 3455 to 3330 (OH), 1760 (γ-lactone), 1697 (*cyclo*pentanone with linear diene conjugation) and 1620 and 1573 cm.$^{-1}$ (C=C, the absorption of lower wave number showing the exaltation for the *cisoid* conformation). The formation of this compound places one (the secondary) hydroxyl vinylogously β with respect to the ketone group of lactucin.

Similar mild alkaline treatment of *iso*tetrahydrolactucin diacetate (VII; R = Ac) gave a dienone-acid (VIII). This showed an ultraviolet band at 281 mμ in keeping with the chromophore postulated. The infrared spectrum disclosed bands at 3375 (OH), 3110 (carboxylic acid), 1735 and 1248 (acetate), 1713 (carboxylic acid), 1680 (*cyclo*pentanone with linear diene conjugation), and 1630 and 1590 (C=C, both bands of normal intensity). The formation of this compound confirms the placing of the γ-lactone grouping with its "alcoholic" oxygen atom in a vinylogously β-position with respect to the ketone group.

In the formation of the acid (VIII) one of the acetate residues is removed by hydrolysis. We presume that this will be the residue attached to the primary hydroxyl group as indicated. The presence of such a primary hydroxyl group has been tacitly assumed so far. Such a group must be present (*a*) because of the *C*-Me content (2 groups) of

[5] *Inter al.*, Hirschmann, Snoddy, Hiskey, and Wendler, *J. Amer. Chem. Soc.*, 1954, **76**, 4013: Wintersteiner and Moore, *ibid.*, 1956, **78**, 6193.
[6] Braude and Timmons, *J.*, 1955, 3766.
[7] Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123; 1942, **64**, 76; Gillam and West, *J.*, 1942, 486.
[8] Beaton, Johnston, McKean, and Spring, *J.*, 1953, 3660; Beaton, Shaw, Spring, Stevenson, Strachan, and Stewart, *J.*, 1955, 2606.

XUM

dihydrolactucin and all of the more hydrogenated compounds including hexahydrolactucin and (*b*) because it is not possible to place an easily esterifiable (and therefore primary or secondary) hydroxyl group at the remaining secondary position in lactucin without its being detected in the chromophore of the " anhydro "-compound (VI). Indeed in this eventuality the latter would, in fact, be an ene-1 : 4-dione and not a dienone.

Reduction of dihydrolactucin diacetate (IV; R = Ac) with zinc dust and acetic anhydride [9] afforded a deacetoxy-compound. This had the same chromophore (ultraviolet absorption spectrum) as dihydrolactucin and, after allowance for the acetate residue, the same *C*-Me content. The infrared spectrum (in $CHCl_3$) disclosed bands at 1780 ($\gamma$-lactone), 1740 and 1238 (acetate), 1693 (C=C·CO·C=C; 5-membered ring), and 1642 and 1618 cm.$^{-1}$ (conjugated C=C, the band of lower wave-number showing the *cisoid* exaltation). The compound must, therefore, be formulated as (XI). We consider that it arises by vinylogous β-elimination of the secondary acetate residue to give an intermediate (X) which is then reduced. In agreement with this suggestion the dienone chromophore of compound (VI) was completely removed under the same reaction conditions.

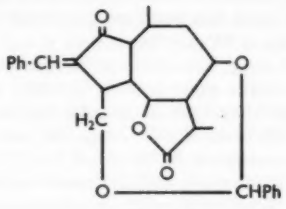
The position of the primary hydroxyl group of lactucin was established by the following experiments. First, ozonolysis of tetrahydrolactucin (V; R = H) afforded a product which gave 0·38 mol. of iodoform when subjected to the iodoform test. *iso*Tetrahydrolactucin (VII; R = H), under the same conditions, gave no iodoform. Secondly, treatment of hexahydrolactucin ditoluene-*p*-sulphonate (II; R = *p*-Me·$C_6H_4$·$SO_2$) with triethylamine furnished a monotoluene-*p*-sulphonate (XI; R = *p*-Me·$C_6H_4$·$SO_2$). This showed infrared bands (in $CHCl_3$) at 1768 ($\gamma$-lactone), 1718 (*cyclo*pentanone conjugated with a *cyclo*propane ring),[10] and 1600 (C=C of toluene-*p*-sulphonate) cm.$^{-1}$ in agreement with the assigned constitution. When tetrahydrolactucin was converted into its ditoluene-*p*-sulphonate (V; R = *p*-Me·$C_6H_4$·$SO_2$) and this treated with triethylamine in the same way, *both* toluene-*p*-sulphonate residues were eliminated to furnish the dienone (XII). This compound, isolated *without* acidification, showed ultraviolet absorption at 238 and 291 mμ (more intense). The spectrum is different from that of the analogous dienone (VI), but not by a degree unexpected in view of the strain introduced by the formation of the *cyclo*propane ring. The infrared spectrum (in $CHCl_3$) exhibited bands at 1773 ($\gamma$-lactone), 1693 (·CO·C=C; 5-membered ring; with " extra " conjugation from the *cyclo*propane ring), 1632 (C=C of normal intensity), and 1590 cm.$^{-1}$ (C=C of exalted intensity due to the *cisoid* conformation), all of which are in agreement with the assigned constitution. A dienone of the type (XII) with the additional *cyclo*propane ring could not, of course, have been formed if the primary hydroxyl group of lactucin had been in the alternative position.

Hexahydrolactucin (II) gave a strongly positive Zimmermann test in agreement with the presence of the grouping $-CH_2$·CO$-$. Furthermore, treatment with benzaldehyde under basic conditions sufficiently mild to leave the $\gamma$-lactone ring intact afforded an amorphous benzylidene ketone with the correct ultraviolet absorption spectrum. Further condensation with benzaldehyde in the presence of acid then furnished a nicely crystalline dibenzylidene derivative (XIII). This had the expected ultraviolet absorption and showed bands in the infrared (in $CHCl_3$) at 1775 ($\gamma$-lactone), 1707 (·CO·C=C; 5-membered ring), 1614 (C=C of exalted intensity due to the *cisoid* conformation), 1577 (aromatic C=C), and 1116 (C–O–C) cm.$^{-1}$. There was no hydroxyl absorption in the infrared spectrum, and the compound was recovered unchanged on attempted acetylation.

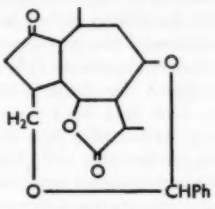
When hexahydrolactucin itself was treated with benzaldehyde in the presence of acid under the same conditions it was recovered unchanged. However, if the hexahydrolactucin were first treated with a mild base it was isomerised to an oily *iso*hexahydrolactucin. This, when warmed with benzaldehyde under the same acid conditions, readily afforded a crystalline benzylidene derivative (XIV). The latter showed infrared maxima

[9] Cf. Woodward, Sondheimer, Taub, Heusler, and McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223.
[10] Eastman, *ibid.*, 1954, **76**, 4115.

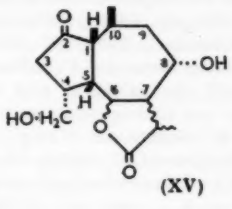
(in $CHCl_3$) at 1777 ($\gamma$-lactone), 1740 (*cyclo*pentanone), 1603 (aromatic C=C), and 1118 (C–O–C) cm.$^{-1}$. There was no hydroxyl absorption.




(XIII)




(XIV)




(XV)

The formation of these benzylidene derivatives throws considerable light on the stereochemistry of hexahydrolactucin. Models show that the benzylidene bridge can be formed only if the stereochemistry at positions 1, 5, and 4, 8 is as shown in formula (XV) (or its mirror image).* If we assume that hydrogenation of the 1 : 10-double bond gives *cis*-hydrogen addition at positions 1 and 10, and further that the isomerisation of hexahydro- to *iso*hexahydro-lactucin involves inversion at position 1, then the 1 : 10-hydrogen atoms in the latter are *trans*-related, giving the orientation at position 10 as in formula (XV) (or its mirror image).

On digestion with methanolic sodium hydroxide lactucin and dihydrolactucin afford formic acid. Tetrahydrolactucin, *iso*tetrahydrolactucin (as judged by acetyl determinations under comparable conditions), the dienone (VI), and hexahydrolactucin gave no formic acid in this way. The formic acid must arise from the primary hydroxyl group. By $\beta\gamma$-shift of a 3 : 4-ethylenic linkage this would be converted into a formyl group. Whenever an ethylenic linkage could be tautomerised to the 1 : 5-position then a vinylogous $\beta$-aldehydo-ketone would result. Such compounds are, of course, subject to ready deformylation by alkali. It is, therefore, not difficult to account for the observed selectivity in the generation of formic acid.

Lactucin is of interest biogenically as the first sesquiterpenoid lactone of the azulene series with a proven carbonyl group at $C_{(2)}$.†

## Experimental

M. p.s were taken on the Kofler block. Unless specified to the contrary, $[\alpha]_D$ are in $CHCl_3$; ultraviolet absorption spectra were determined in EtOH on the Unicam S.P. 500 Spectrophotometer. Infrared spectra were kindly determined by Dr. G. Eglinton and his colleagues. The alumina for chromatography was acid-washed, neutralised, and standardised according to Brockmann's method.[13] Unless stated to the contrary the light petroleum used was of b. p. 60—80°. Microanalyses were carried out by Mr. J. M. L. Cameron and his associates.

*Lactucin.*—The bitter principle was extracted from crude lactucarium, essentially by the method of Späth, Schenck, and Schreber.[14] Recrystallised from acetone, methanol or ethyl acetate, it had m. p. 213—217°, $[\alpha]_D$ +49° (*c* 0·90 in MeOH), +69° (*c* 0·98 in pyridine), $\lambda_{max.}$ 257 m$\mu$ ($\varepsilon$ 14,000) (Found: C, 65·35; H, 6·05; *C*-Me, 8·6, 5·3, 8·9. Calc. for $C_{15}H_{16}O_5$: C, 65·2; H, 5·85; *C*-Me, 5·45%). Lactucin gives no colour with ferric chloride solution. It developed

* For the numbering used for these lactones see Barton, de Mayo, and Shafiq, *J.*, 1957, 929.

† Braun, Herz, and Rabindran [11] have suggested that tenulin also possesses this feature, although, of course, the earlier work of Barton and de Mayo [12] excludes such a possibility. In a personal communication Professor Herz (Florida State University) has very kindly informed us that he now accepts the 3-position for the ketonic group in tenulin.

[11] Braun, Herz, and Rabindran, *J. Amer. Chem. Soc.*, 1956, **78**, 4423.
[12] Barton and de Mayo, *J.*, 1956, 142.
[13] Brockmann and Schodder, *Ber.*, 1941, **74**, 73.
[14] Späth, Schenck, and Schreber, *Arch. Pharm.*, 1939, **277**, 203.

a strong colour in 2·5% ethanolic potassium hydroxide, the spectrum showing $\lambda_{max.}$ 430 mμ (ε 13,200; maximum intensity) after 30 minutes at room temperature. During the development of this chromophore the original band at 257 mμ disappeared.

Treatment with pyridine–acetic anhydride for 6 hr. at room temperature gave lactucin diacetate, m. p. 159—163° (from acetone–light petroleum), $[\alpha]_D$ +87° (*c* 0·74).

*Dihydrolactucin.*—Palladised calcium carbonate (1%; 117 mg.), suspended in 95% ethanol (10 ml.), was saturated with hydrogen. Lactucin (1·38 g.) in the same solvent (70 ml.) was added and hydrogenated until one mol. had been consumed. Crystallisation from methanol gave *dihydrolactucin* (1·14 g.), m. p. 176—180°, $[\alpha]_D$ +6° (*c* 0·74 in MeOH), $\lambda_{max.}$ 257 mμ (ε 15,000) (Found: C, 64·95; H, 6·25; *C*-Me, 10·1. $C_{15}H_{18}O_5$ requires C, 64·75; H, 6·5; 2*C*-Me, 10·8%). Dihydrolactucin gave the same colour reaction as lactucin in 2·5% ethanolic alkali, showing $\lambda_{max.}$ 430 mμ (ε 10,800; maximum intensity). Treatment with pyridine–acetic anhydride at room temperature for 6 hr. gave *dihydrolactucin diacetate*, m. p. (from methanol) 204—208°, $[\alpha]_D$ +20° (*c* 0·89) (Found: C, 63·0; H, 6·1; *C*-Me, 15·8. $C_{19}H_{22}O_7$ requires C, 62·95; H, 6·1; 4*C*-Me, 16·6%).

*Tetrahydrolactucin.*—(a) *Hydrogenation of dihydrolactucin.* Palladised calcium carbonate (1%; 136 mg.), suspended in 95% ethanol (10 ml.), was saturated with hydrogen. Dihydrolactucin (600 mg.) in the same solvent (70 ml.) was added and hydrogenated until 1 mol. had been consumed. Crystallisation from ethyl acetate furnished *tetrahydrolactucin* (69 mg.), m. p. 293—295°, $[\alpha]_D$ +6° (*c* 0·68 in pyridine), $\lambda_{max.}$ 252 (ε 11,000) (Found: C, 64·05; H, 7·05; *C*-Me, 10·0. $C_{15}H_{20}O_5$ requires C, 64·25; H, 7·2; 2*C*-Me, 10·75%).

(b) *Hydrogenation of lactucin.* Palladised calcium carbonate (1%; 350 mg.), suspended in 95% ethanol (10 ml.), was saturated with hydrogen. Lactucin (1·38 g.) in 95% ethanol (70 ml.) was added and hydrogenated until 2 mol. had been consumed. Crystallisation as above gave the same tetrahydrolactucin (270 mg.), affording, as above, a *diacetate*, m. p. (from acetone–light petroleum) 138—140°, $[\alpha]_D$ −14° (*c* 1·10) (Found: C, 62·85; H, 6·7; Ac, 23·35. $C_{19}H_{24}O_7$ requires C, 62·6; H, 6·65; Ac, 23·6%).

iso*Tetrahydrolactucin.*—The oily residues remaining after crystallisation of tetrahydrolactucin (obtained from either lactucin or dihydrolactucin) contained an isomeric compound showing $\lambda_{max.}$ 227 mμ. This was separated as follows. The oily material (3·6 g.) in pyridine (18 ml.) and acetic anhydride (18 ml.) was kept at room temperature for 7 hr. The crude acetate was chromatographed over silica (160 g.) in benzene solution. The first 15 eluates (500 ml. portions) contained mixtures of dihydro- and tetrahydro-lactucin diacetate. Fractions 18 to 20, eluted with 5, 10, and 25% ether–benzene respectively consisted mainly of the desired material (ultraviolet spectrum). Crystallisation of these combined fractions from carbon tetrachloride and then from acetone gave iso*tetrahydrolactucin diacetate* (180 mg.), m. p. (needles from acetone) 176—180°, $[\alpha]_D$ +127° (*c* 1·00), $\lambda_{max.}$ 227 mμ (ε 8500) (Found: C, 62·5; H, 6·5; Ac, 23·1. $C_{19}H_{24}O_7$ requires C, 62·6; H, 6·65; Ac, 23·6%).

*Hexahydrolactucin.*—Complete hydrogenation of lactucin using palladised charcoal (5%) in 95% ethanol gave the known [2,3] hexahydrolactucin, m. p. (from ethyl acetate) 180—182°, $[\alpha]_D$ +95° (*c* 0·66 in MeOH), +85° (*c* 0·72 in pyridine) (Found: C, 63·75; H, 7·85; *C*-Me, 10·25. Calc. for $C_{15}H_{22}O_5$: C, 63·8; H, 7·85; 2*C*-Me, 10·65%). The same compound (m. p., mixed m. p., rotation, and infrared spectrum) resulted from the hydrogenation of tetrahydrolactucin under the same conditions. A Zimmermann test on hexahydrolactucin was strongly positive.

Treatment of hexahydrolactucin (300 mg.) in dry pyridine (25 ml.) with purified toluene-*p*-sulphonyl chloride (2·46 g.) at room temperature for 16 hr. gave *hexahydrolactucin ditoluene-p-sulphonate* (143 mg.), m. p. (from acetone) 152—153°, $[\alpha]_D$ +33° (*c* 0·52), $\lambda_{max.}$ 226 mμ (ε 21,000) (Found: C, 59·1; H, 6·25; S, 10·1. $C_{29}H_{34}O_9S_2$ requires C, 58·95; H, 5·8; S, 10·85%). The infrared spectrum (Nujol) showed bands at 1773 (γ-lactone), 1733 (*cyclo*pentanone), 1596 (aromatic C=C) and 1172 ($C_6H_4Me{\cdot}SO_3$) cm.$^{-1}$.

*Treatment of Hexahydrolactucin Ditoluene-p-sulphonate with Triethylamine.*—The ditoluene-*p*-sulphonate (200 mg.) was refluxed with anhydrous triethylamine (dried over Na wire) (20 ml.) for 11 hr. The triethylamine was removed *in vacuo* and the residue dissolved in chloroform and washed with 0·5N-hydrochloric acid and then with saturated aqueous sodium hydrogen carbonate. Crystallisation from acetone–light petroleum afforded the *monotoluene-p-sulphonate* (XI; R = toluene-*p*-sulphonyl) (rectangular plates) (90 mg.), m. p. 201—203°, $[\alpha]_D$ +55° (*c* 0·60), $\lambda_{max.}$ 226 mμ (ε 7200) (Found: C, 62·95; H, 6·05; S, 7·5. $C_{22}H_{26}O_6S$ requires C, 63·15; H, 6·25; S, 7·65%). This compound gave a negative Zimmermann test.

*Tetrahydrolactucin Ditoluene-p-sulphonate and its Reaction with Triethylamine.*—Tetrahydrolactucin, treated with toluene-*p*-sulphonyl chloride as for the hexahydro-derivative (see above), gave *tetrahydrolactucin ditoluene-p-sulphonate*. Recrystallised from alcohol and then from acetone–light petroleum this (thin plates) had m. p. 156—157°, $[\alpha]_D$ −33° (*c* 0·80), $\lambda_{max.}$ 226 and 250 mμ (ε 29,000 and 13,000 respectively), infrared maxima ($CHCl_3$) at 1775 (γ-lactone), 1708 (*cyclo*pentenone), 1613 (strong; *cisoid* C=C conjugated with ketone), 1598 (aromatic C=C), and 1175 cm.$^{-1}$ (toluene-*p*-sulphonate) (Found: C, 59·35; H, 5·8; S, 10·45. $C_{29}H_{32}O_9S_2$ requires C, 59·15; H, 5·5; S, 10·9%).

The ditoluene-*p*-sulphonate (520 mg.) was refluxed with anhydrous triethylamine (200 ml.) for 11 hr. (spectrophotometric control). The triethylamine was removed *in vacuo* and the residue extracted into ether and washed with saturated sodium hydrogen carbonate solution. The product was chromatographed in benzene over alumina (Grade III; 5 g.), elution being with benzene. Crystallisation from acetone–light petroleum afforded the desired *dienone* (XII) (200 mg.), m. p. (after sublimation) 157—162°, $[\alpha]_D$ +142° (*c* 0·62), $\lambda_{max.}$ 238 and 291 mμ (ε 4500 and 9800 respectively) (Found: C, 73·75; H, 6·65. $C_{15}H_{16}O_3$ requires C, 73·75; H, 6·6%).

*Ozonolyses.*—(*a*) Lactucin (138 mg.) in anhydrous tetrahydrofuran (40 ml.) was ozonised at −40° to −60° for 75 min. (disappearance of ultraviolet band at 258 mμ). Addition of water and steam-distillation into aqueous dimedone solution gave the formaldehyde dimedone derivative (42 mg. crude; 34 mg. pure; 23%), identified by m. p. and mixed m. p.

(*b*) Dihydrolactucin, ozonised under the same conditions, gave no formaldehyde dimedone derivative.

(*c*) Tetrahydrolactucin (100 mg.) in methanol (60 ml.) was ozonised at −50° to −70° until the ultraviolet absorption at 251 mμ had disappeared (100 min.). Water (5 ml.) was added and the solution evaporated to dryness *in vacuo* on the steam-bath. The residue was subjected to the iodoform test as described by Fieser,[15] to furnish iodoform (52 mg., 38%), identified by m. p. and mixed m. p. The appropriate controls, run at the same time, gave no iodoform. Acetophenone (50 mg.) tested also under the same conditions gave iodoform (107 mg., 65%).

(*d*) *iso*Tetrahydrolactucin (100 mg.) in chloroform (40 ml.) was ozonised at −50° to −60° until the ultraviolet max. at 227 mμ had disappeared (60 min.). Water (5 ml.) was added and the mixture of solvents removed *in vacuo*. The residue gave no iodoform when tested as above.

*Treatment of Lactucin and its Derivatives with Alkali.*—Lactucin (305 mg.) was refluxed with methanolic sodium hydroxide (N; 116 ml.) for 3 hr. The methanol was purified first by refluxing it with solid potassium hydroxide then by rectification. The appropriate control was also run. Most of the methanol was removed by distillation. Sulphuric acid (45 ml.; 2 : 1 water : $H_2SO_4$) was added and the volatile acid steam-distilled and titrated with 0·1N-sodium hydroxide (0·4 equiv. of acid). The volatile acid was characterised as formic acid by the infrared spectrum of its sodium salt.

A similar determination on dihydrolactucin gave 0·95 mol. of formic acid. In contrast tetrahydrolactucin, the dienone (VI), and hexahydrolactucin did not furnish formic acid under these conditions.

The formation of excess of volatile acid under acetyl-determination conditions also indicated the presence of formic acid. Thus acetyl determinations on lactucin and dihydrolactucin, carried out with preliminary alkali treatment,[16] gave 30·75 and 28·55% of Ac instead of the theoretical figures of 23·9 and 23·75% respectively.

*Dehydrogenation of Lactucin.*—Lactucin (2·0 g.) in " AnalaR " acetic acid containing 72% aqueous perchloric acid (5 drops) was hydrogenated over platinum (600 mg.). The gummy product (1·5 g.) was dehydrogenated in portions (200 mg.) by 10% palladised charcoal (200 mg.) for 15 min. under nitrogen at 320°. The combined batches were extracted with light petroleum and the blue solution was filtered through alumina (6 g.; Brockmann No. 5). Extraction into 80% phosphoric acid and further treatment in the usual way gave chamazulene (6 mg.), characterised as its trinitrobenzene adduct (m. p., mixed m. p., ultraviolet and visible absorption spectra).

*Dienone from Tetrahydrolactucin.*—Tetrahydrolactucin (300 mg.) in 95% ethanol (63 ml.)

[15] Fieser, " Experiments in Organic Chemistry," 3rd Edn., Heath, Boston, 1955, p. 86.

[16] Pregl's " Quantitative Organic Micro-Analysis," Ed. J. Grant, 5th Edn., J. and A. Churchill Ltd., London, 1951, p. 202.

XUM

was treated with 5% ethanolic potassium hydroxide (7 ml.) at room temperature. The ultraviolet absorption of this solution developed a maximum at 305 mμ (measured against the appropriate control) which reached its highest intensity after 6 hr. Crystallisation of the neutral product, obtained *without* acidification, from acetone–light petroleum gave the *dienone* (VI) (171 mg.) as rectangular prisms, m. p. 207—209°, $[\alpha]_D$ −240° (*c* 0·56), $\lambda_{max.}$ 301 mμ (ε 12,300) (Found: C, 68·8; H, 6·75. $C_{18}H_{18}O_4$ requires C, 68·7; H, 6·9%). When this compound (35 mg.) was refluxed with zinc dust (750 mg.) in dry acetic anhydride (2·5 ml.) under nitrogen with good stirring for 10 min. it gave a product (20 mg.) showing no ultraviolet absorption at 303 mμ, but instead a band at 243 mμ.

*Dienone from* iso*Tetrahydrolactucin Diacetate.*—*iso*Tetrahydrolactucin diacetate (162 mg.) in 95% ethanol (9 ml.) was treated with 5% ethanolic potassium hydroxide (1·0 ml.) at room temperature for 30 min. The reaction was controlled spectrophotometrically as above, to give the optimum conditions. The acidic product was crystallised from chloroform or from acetone–light petroleum, to furnish the *dienone* (VIII) (72 mg. crude; 30 mg. pure), m. p. 200—205° after sintering at 190°, $[\alpha]_D$ +219° (*c* 0·90 in MeOH), $\lambda_{max.}$ 281 mμ (ε 14,000) (Found: C, 63·2; H, 6·6; Ac, 13·85. $C_{17}H_{22}O_6$ requires C, 63·35; H, 6·9; 1Ac, 13·35%). The compound effervesced briskly in sodium hydrogen carbonate solution.

*Reduction of Dihydrolactucin Diacetate with Zinc Dust and Acetic Anhydride.*—Dihydrolactucin diacetate (300 mg.) in dry acetic anhydride (6 ml.) was refluxed under nitrogen with dry zinc dust (3·0 g.; added in one portion) with vigorous stirring for 8—10 min. The oily product (269 mg.) was chromatographed over silica gel (20 g.). Elution with benzene (50 ml. portions) gave 12 fractions showing acetate infrared bands of reduced intensity (relative to the intensity of the γ-lactone carbonyl). Fractions 3—11 were combined (147 mg.) and crystallised from methanol, to afford *deoxydihydrolactucin acetate*, m. p. 188—190°, $[\alpha]_D$ +15° (*c* 0·92), $\lambda_{max.}$ 258 mμ (ε 15,000) (Found: C, 66·95; H, 6·7; *C*-Me, 14·4. $C_{17}H_{20}O_5$ requires C, 67·1; H, 6·6; 3*C*-Me, 14·8%). An acetyl determination showed Ac, 20·75 instead of the theoretical 14·15%. The excess of " acetyl " must again be due to the generation of formic acid (see above).

iso*Hexahydrolactucin and its Derivatives.*—Hexahydrolactucin (106 mg.) in 95% ethanol (5·5 ml.) was treated with ethanolic potassium hydroxide (5% w/v; 0·1 ml.) at room temperature in a polarimeter tube. After 5 min. $[\alpha]_D$ was −50°; after 3 hr. it was constant at −63°. The solution was poured into water (90 ml.) and, without acidification, was extracted with chloroform (10 × 25 ml.). The chloroform extract, after being washed with water (2 × 10 ml.) and dried ($Na_2SO_4$), afforded a neutral product (42 mg.) which did not crystallise. It is regarded as *iso*hexahydrolactucin on the basis of its physical properties {$[\alpha]_D$ −108° (*c* 2·50), no high-intensity ultraviolet absorption, infrared bands ($CHCl_3$) at 3340 (OH), 1760 (γ-lactone), and 1730 (*cyclo*pentanone) cm.$^{-1}$} and of its further chemical reactions (see below).

Treatment of the oily *iso*hexahydrolactucin (135 mg.) in redistilled benzaldehyde (0·6 ml.) on the steam-bath with 6N-aqueous hydrochloric acid (2 drops) for 2 min., followed by removal of excess of benzaldehyde at steam-bath temperature *in vacuo*, gave the iso*hexahydrolactucin* OO-*benzylidene derivative* (XIV). Recrystallised from acetone–light petroleum this (59 mg.) had m. p. (cubes) 266—268°, $[\alpha]_D$ −143° (*c* 0·86) (Found: C, 71·1; H, 6·95. $C_{22}H_{26}O_5$ requires C, 71·35; H, 7·1%). Hexahydrolactucin, itself, was recovered unchanged under the same conditions.

The condensation of benzaldehyde with *iso*hexahydrolactucin under alkaline conditions was also investigated. *iso*Hexahydrolactucin (390 mg.) in absolute ethanol (10 ml.) was treated with redistilled benzaldehyde (2·4 ml.) and ethanolic potassium hydroxide (5% w/v; 0·2 ml.) at room temperature for 23 hr. (spectrophotometric control using the band at 300 mμ). The neutral product was chromatographed over alumina (13 fractions). The (five) fractions showing the correct ultraviolet and infrared bands for a benzylidene derivative were combined. They showed $[\alpha]_D$ −11° (*c* 0·80), $\lambda_{max.}$ 300 mμ (ε 16,000), infrared bands at 3363 (OH), 1760 (γ-lactone), 1704 (*cyclo*pentenone), 1615 (strong *cisoid* C=C), and 1580 (aromatic C=C) cm.$^{-1}$ and consisted of essentially pure benzylidene derivative. This compound (90 mg.) in benzaldehyde (0·6 ml.) was heated on the steam-bath with 6N-aqueous hydrochloric acid (2 drops) for 2 min. Working up as in the comparable example above afforded the iso*hexahydrolactucin dibenzylidene derivative* (XIII). Recrystallized from acetone–light petroleum this formed rectangular prisms, m. p. 287—289°, $[\alpha]_D$ −72° (*c* 0·83), $\lambda_{max.}$ 300 mμ (ε 17,600) (Found: C, 76·1; H, 6·75. $C_{29}H_{30}O_5$ requires C, 75·95; H, 6·6%). Treatment of crude benzylidene compound gave the same dibenzylidene derivative without any difficulty. The dibenzylidene derivative could not be acetylated under normal conditions.

We thank the D.S.I.R., the Government Grants Committee of the Royal Society, and Imperial Chemical Industries Limited, for financial assistance. We are grateful to Messrs. Glaxo Laboratories Ltd. for the large-scale extraction of lactucarium. One of us (C. R. N.) is indebted to the University of Glasgow for a Research Fellowship. The Editor kindly made some helpful comments on the manuscript of this paper.

THE UNIVERSITY, GLASGOW, W.2.
IMPERIAL COLLEGE, LONDON, S.W.7.

[*Received, October 18th*, 1957.]

## 195. *The Light Absorption of Pyrroles. Part II.* Infrared Spectra.*

By ULLI EISNER and R. L. ERSKINE.

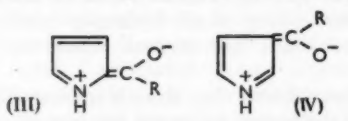
The infrared spectra of a number of pyrroles have been measured. The relation between structure and N–H and C=O frequencies is discussed. A band in the 1470—1600 cm.$^{-1}$ region, present in all the pyrroles examined, is assigned to bond-stretching vibrations of the ring.

THE infrared and Raman spectra of substituted pyrroles show some anomalies, particularly a lowering of the C=O stretching frequency in carbonyl-substituted pyrroles. Although data for a number of pyrroles have been recorded [1-9] comparatively little has been done to interpret the results and establish correlations. Since a number of pyrroles were available to us, their infrared spectra have been determined. The present work, however, is not a systematic study since there are not sufficient data for mono- and di-substituted derivatives.

The carbonyl-stretching frequency of αβ-unsaturated β-amino-ketones (I) occurs at lower frequencies than that of ordinary αβ-unsaturated ketones as the nitrogen atom

(I) $R^1R^2N{\cdot}CH{=}CH{\cdot}COR^3$ $\quad R^1R^2N^+{=}CH{\cdot}CH{=}CR^3{\cdot}O^-$ (II)

stabilises the dipolar form [10] (II). Carbonyl-substituted pyrroles can also exist in dipolar forms (III, IV) which shift the carbonyl band to lower frequencies, 2- and 3-carbonyl



(III) (IV)

substituents being similarly affected. The hydrogen atom on the nitrogen is not essential for this perturbation [1,4,7,10] and this has been confirmed in our work, since the 1-methylpyrrole (17 †) has the same carbonyl-stretching frequency as the 1-unsubstituted analogue (16). Intramolecular hydrogen bonding is excluded in the 2-substituted compounds (see below).

Furan and thiophen derivatives containing carbonyl substituents show similar shifts [3,11,12] which are less pronounced than those observed for the corresponding pyrroles.

* Part I, *J.*, 1958, 922.
† This and similar Arabic numbers in parentheses refer to the numbers in the Table.

[1] Ansidei, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1940, **11**, 669.
[2] Bonino and Chiorboli, *ibid.*, 1951, **10**, 104.
[3] Chiorboli, *ibid.*, 1952, **12**, 92, 558.
[4] Bonino and Mirone, *ibid.*, 1954, **17**, 167, 254.
[5] Mirone, Drusiani, and Lorenzelli, *Ann. Chim.* (*Italy*), 1956, **46**, 1217.
[6] Nicolaus and Oriente, *Gazzetta*, 1954, **84**, 230.
[7] Nicolaus and Mangoni, *ibid.*, 1955, **85**, 1378.
[8] Scrocco and Nicolaus, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1956, **20**, 795.
[9] *Idem, ibid.*, 1956, **21**, 103.
[10] Cromwell, Miller, Johnson, Frank, and Wallace, *J. Amer. Chem. Soc.*, 1949, **71**, 3337.
[11] Mirone, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1954, **16**, 483.
[12] Chiorboli and Mirone, *ibid.*, p. 243.

XUM

The infrared measurements for chloroform solution and for the solid state are summarised in the Table. This shows separately the N–H bands, bands in the C=O stretching region and at 1600—1475 cm.$^{-1}$, and other marked bands in the " finger-print " region. The apparent maximal extinction coefficients are given in parentheses for measurements on solutions representing intensities more accurately than the symbols s(strong), m(medium), and w(weak). The estimated error is about $\pm 5\%$, and all measurements were made from the 100% $T$ line except for the " free " NH band where some attempt was made to cancel out the absorption due to the " bonded " NH band when this was present.

The solid-state spectra (paraffin mulls) showed a marked inconsistency between very similar compounds which must be due to the intermolecular bonding effects in the crystals. This was especially noticeable in the pairs (13) and (14), and (5) and (6), where the difference in structure was due only to the alkyl substituents. Consequently identification of these compounds from their solid-state spectra is not to be recommended and only solution spectra give consistent results.

The discussion of the spectra therefore concerns solution results unless otherwise indicated. Bands in the 3000—2775 and 1480—1330 cm.$^{-1}$ ranges are not quoted because they were masked by solvent bands in solution and by the C–H bands in paraffin. Similarly bands below 800 cm.$^{-1}$ for chloroform solution are not recorded owing to the absorption of the solvent.

*The* N–H *Stretching Region.*—In chloroform solution the N–H absorption appears as a sharp band in the range 3435—3400 cm.$^{-1}$. The N–H stretching frequency of pyrrole itself in carbon tetrachloride is a little higher at 3488 cm.$^{-1}$; there appears to be a small solvent effect as this frequency is lowered by 13 cm.$^{-1}$ in chloroform solution. Since the N–H stretching frequency is not appreciably altered by the presence of 2-carbonyl substituents, intramolecular hydrogen bonding is ruled out and this absorption is therefore due to the " free " N–H group.

In the solid state the N–H stretching frequency occurs in a much wider range at lower frequencies, *viz.*, 3315—3085 cm.$^{-1}$. There is no apparent relation between the position of this bonded N–H absorption and the chemical nature of the substituents, although large 2-substituents [cf. compounds (7), (13), (14), (22)] seem to hinder intermolecular hydrogen bonding of the N–H group, giving weak hydrogen bonds with higher frequencies, whereas stronger hydrogen bonds are formed when the 2-substituents are small [cf. (15), (12)].

Scrocco and Nicolaus [9] have shown that there is a linear relationship between the p$K_a$ value of the pyrrole and the difference, $\Delta\nu$, in the frequency of the free and bonded N–H vibrations, both determined in solution. While we have not determined any p$K_a$ values, our $\Delta\nu$ values correspond in magnitude to those given by Scrocco and Nicolaus. In those spectra where the bonded N–H band was visible, the largest $\Delta\nu$ value was given by compound (37) with 210 cm.$^{-1}$ and the smallest by (3) with 115 cm.$^{-1}$.

Our determinations were made with a rock-salt prism and the estimated error in frequency is about $\pm 10$ cm.$^{-1}$ so that the extent of the range of the N–H frequency, particularly in solution, is probably due to experimental error rather than to real differences in the positions of the N–H stretching frequencies. As a check on the accuracy of our results the N–H frequency of pyrrole was redetermined; it was found to be in excellent agreement with the results recorded by Fuson.[13] A discrepancy was noted between our results and those of Scrocco and Nicolaus [9] for pyrroles (16) and (31) even after corrections for solvent effect were made. Similarly our N–H frequencies were found to be lower than the values recorded by Mirone *et al.*[5] for pyrroles (28), (29), and (31). Since the above workers used a lithium fluoride prism it is likely that the differences observed are due to this.

*The Carbonyl Stretching Region.*—A comparison of the solution and the solid-state spectra in the carbonyl-stretching region near 1670 cm.$^{-1}$ shows a marked dissimilarity in

[13] Fuson, Josien, Powell, and Utterback, *J. Chem. Phys.*, 1952, **20**, 145.

the absorption. This is probably due to intermolecular N–H · · · O=C hydrogen bonding and consequently solid-state spectra do not give consistent results even among similar compounds as the carbonyl-stretching frequency depends on the packing and hydrogen bonding in the crystals. Mirone, Drusiani, and Lorenzelli [5] have found similar inconsistencies in a series of substituted pyrrole aldehydes. The solution spectra give much more consistent results which will now be discussed.

The pyrrolic monoesters (4), (5), (6), and (10) have essentially the same carbonyl-stretching frequency irrespective of whether the ester group is in the 2- or 3-position. This indicates that the dipolar forms (III) and (IV) can be formed with equal ease, and hence that it is not possible to determine the position of a pyrrolic carbonyl substituent from the C=O stretching frequency. Similarly the C=O frequency of the 2-acetyl derivative (11) lies very close to that of the 3-acetylpyrrole (12). The ketones absorb at a frequency about 40 cm.$^{-1}$ lower than that of the esters, the shift being of the same order as that observed in normal ketones and esters.

Pyrroles carrying two ester groups, (13—17), give rise to one asymmetrical carbonyl-stretching band. This is probably due to the fact that the two ester groups absorb at frequencies very close to each other so that the bands are not resolved. As both the symmetrical 2 : 5-diesters (13), (14), and the 3 : 4-diester (15) have asymmetric carbonyl bands, there must be weak mechanical interaction between the two vibrations rather than preferential perturbation of one of the ester groups which might be postulated, for example, with diethyl 2 : 4-dimethylpyrrole-3 : 5-dicarboxylate (16). Mechanical interaction would be strongest when the two ester groups are in adjacent positions in the ring and this is confirmed by our data, although the triester (30) appears to be abnormal in this respect.

The spectrum of one 1-substituted pyrrole (17) was recorded to confirm (cf. refs. 1, 4, 7) that the hydrogen attached to the nitrogen atom is not essential for the perturbation, and to rule out the possibility of hydrogen bonding between the N–H group and adjacent 2-carboxyl substituent. The carbonyl-stretching frequency of diethyl 1 : 2 : 4-trimethylpyrrole-3 : 5-dicarboxylate (17) is identical with that of diethyl 2 : 4-dimethylpyrrole-3 : 5-dicarboxylate (16).

Pyrroles (23—29), containing both ester and carbonyl groups, have a much more complex absorption, giving rise to two, and sometimes three or more, bands. Mirone *et al.*[5] have differentiated four types of carbonyl frequencies in a series of pyrrolic ester-aldehydes in the solid state which are called " associated " and " unassociated " ester and aldehyde bands, but there is not sufficient evidence in our work for such a definitive assignment.

The dipyrrylmethanes (8) and (9) show the expected shift of the carbonyl band in solution, but in the solid state strong intermolecular hydrogen-bonding splits the bands into two sharp maxima at 1688, 1644 cm.$^{-1}$ and 1699, 1647 cm.$^{-1}$ respectively.

The pyrrolic nitriles (36—40) absorb normally and there appears to be no effect of the pyrrole ring on the stretching frequency of the C≡N group. This frequency at about 2230 cm.$^{-1}$ is comparable with the C≡N stretching frequency of benzonitrile [14] also at 2230 cm.$^{-1}$.

The effect of alkyl substituents on the C=O frequency has not been fully elucidated, chiefly owing to the lack of data. Mirone *et al.*[5] found that, in the solid state, the C=O frequency is lowered by increasing alkyl-substitution. We have confirmed this effect in the case of the trisubstituted monoester (4) which absorbs at 1678 cm.$^{-1}$ and the tetra-substituted monoesters (5) and (6) which absorb at 1669 cm.$^{-1}$ in chloroform. However, there is a slight increase in the C≡N band when going from the trisubstituted nitrile (36) (2229 cm.$^{-1}$) to the tetrasubstituted derivatives (37) and (38) which absorb at 2237 and 2234 cm.$^{-1}$ respectively.

*The* 1600—1470 *cm.*$^{-1}$ *Region.*—All the compounds which have been examined have absorption in the 1600—1470 cm.$^{-1}$ region which generally consists of two bands of variable intensity and position. In most cases, one band was near 1565 cm.$^{-1}$ and the other near

[14] Kitson and Griffith, *Analyt. Chem.*, 1952, **24**, 334.

*Infrared maxima (cm.$^{-1}$) of pyrroles* (C = in $CHCl_3$, N = in Nujol)

| No. | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | | N–H stretching | C=O stretching | 1600—1475 | Other bands |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | H | H | H | H | H | C | 3475 [a] | — | — | — |
| 2 | H | H | Et | Et | H | — | 3370s [b] | — | 1564w 1516w | 1070s 1035m 950w 891m 797m 778m |
| 3 | H | [c] | Et | Et | H | C | 3425m 3310m | — | 1623m | 1299m 1154w 1113m 1088m 1049m 985w 877w |
| 4 | H | $CO_2Et$ | Me | H | Me | C | 3435(117) | 1678(500) | 1585(77) 1548(84) | 1100(307) 1020(52) 1011(59) 928(62) |
| | | | | | | N | 3251m | 1657s | 1575w 1545w 1495w | 1269s 1215s 1101s 1025m 801s |
| 5 | H | $CO_2Et$ | Me | Me | Me | C | 3420(119) | 1669(456) | 1585(35) 1497(171) | 1323(106) 1110(260) 1065(161) 926(125) |
| | | | | | | N | 3241m | 1668s | 1548w 1499w | 1271s 1223m 1175m 1121m 1112m 1025m 773s 761s |
| 6 | H | $CO_2Et$ | Et | Et | Me | C | 3420(115) | 1669(569) | 1576(55) 1493(171) | 1120(284) 1095(149) 1083(218) 1022(189) |
| | | | | | | N | 3448w 3273m | 1709w 1664s | 1496m | 1277s 1259s 1170m 1122m 1098m 1029m 776m |
| 7 | H | $CO_2Et$ | Me | Me | $CH_2{\cdot}OMe$ | N | 3257m | 1669s | 1545w 1497w | 1270s 1245s 1121s 1085s 1021m 951m 774m 740m |
| 8 | Substance A [d] | | | — | — | C | 3415(125) 3290(63) | 1674(880) | 1600(71) 1580(71) 1493sh | 1297(265) 1151(218) 1096(352) 1064(234) 941(71) |
| | | | | | | N | 3315m | 1688s 1644s | 1581w 1501sh | 1308s 1279s 1260s 1221s 1134s 1103m 768m 675w |
| 9 | Substance B [e] | | | — | — | C | 3420(166) 3290sh | 1680(1060) | 1603(106) 1580(71) 1493sh | 1299(310) 1152(267) 1111(297) 1072(356) 1017(115) |
| | | | | | | N | 3305m | 1694s 1647s | 1577w 1501sh | 1302m 1280s 1254s 1224m 1139s 1110m 1083m 1019m 768m 723w |
| 10 | H | Me | $CO_2Et$ | Me | H | C | 3420(125) 3268(14) | 1683(538) | 1575(53) 1511(41) | 1319(233) 1116(385) 1079(310) |
| | | | | | | N | 3273m | 1667s | 1580m 1521 } dbt w 1506 } | 1326m 1264s 1131s 1093s 1019m 788m 745m 733s |
| 11 | H | Ac | H | H | H | C | 3420(122) 3236(22) | 1642(439) | 1538(105) 1508(57) | 1316(173) 1140(87) 1109(180) 1038(137) 925(56) |
| | | | | | | N | 3210m | 1639s | 1542m 1501w | 1140m 1127m 1042m 972m 926m 841m 773s 750s |
| 12 | H | Me | Ac | Me | H | C | 3435(80) 3250(43) | 1637(437) | 1563(105) | 1325(66) 1052(43) 941(123) |
| | | | | | | N | 3190m | 1617s | 1576w 1508w | 1239m 1071w 1021w 943m 752m |
| 13 | H | $CO_2Et$ | Me | Me | $CO_2Et$ | C | 3420(130) | 1691(841) | 1565(73) 1499sh | 1140(400) 1091(263) 1017(142) |
| | | | | | | N | 3450w 3250m | 1714 } dbt s 1702 } | 1564w 1505sh | 1269s 1253s 1193m 1138m 1019m 783m |
| 14 | H | $CO_2Me$ | Et | Et | $CO_2Me$ | C | 3425(137) | 1707(920) | 1560(134) | 1143(335) 1087(246) 1062(83) 1016(61) 983(77) |
| | | | | | | N | 3425w 3245m | 1718sh 1700s | 1546m | 1254s 1135m 1085m 982m 786s |
| 15 | H | H | $CO_2Et$ | $CO_2Et$ | H | C | 3430(125) 3265(51) | 1723(565) 1695sh | 1519(152) | 1326(279) 1286(635) 1175(302) 1134(231) 1058(538) |
| | | | | | | N | 3205m | 1711s 1694sh | 1526m | 1284s 1197m 1136m 1055s 813m 768s |
| 16 | H | Me | $CO_2Et$ | Me | $CO_2Et$ | C | 3420(116) 3265(20) | 1681(764) | 1572(164) 1504(155) | 1111(208) 1085(452) 1073(445) 1018(87) |
| | | | | | | N | 3210m | 1686 } dbt s 1668 } | 1570w 1506w | 1260s 1195s 1086s 1025m 893m 787m 773m |
| 17 | Me | Me | $CO_2Et$ | Me | $CO_2Et$ | C | — | 1681(1030) | 1541(144) 1477(224) | 1152(496) 1110(385) 1091(534) 1048(106) |
| | | | | | | N | — | 1691s | 1535m 1483sh | 1262s 1244s 1160m 1121m 1107m 1082m 786w |
| 18 | H | $CHCl_2$ | $CO_2Et$ | Me | $CO_2Et$ | C | 3400(113) | 1718sh 1691(782) | 1564(153) 1473(210) | 1284(471) 1113(160) 1073(434) 1014(119) |
| 19 | H | $CO_2Et$ | $CO_2Et$ | H | Me | N | 3245m | 1721s 1665s | 1579w 1494m | 1276s 1235m 1206s 1072s 1024m 850m 776m |

XUM

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 19 | H | $CO_2Et$ | $CO_2Et$ | H | Me | N | 3245m | 1721s 1665s | 1579w 1494m | 1276s 1235m 1206s 1072s 1024m 850m 776m |
| 20 | H | $CO_2Et$ | $CO_2Et$ | Me | Me | N | 3250m | 1702m 1660s | 1574w 1493w | 1258s 1082m 1028m 790m 778m 731m |
| 21 | H | $CO_2Et$ | $CO_2Et$ | Br | Me | N | 3210m | 1733s 1681s | 1574w 1528m | 1275s 1238m 1207s 1079m 1053m 1025m 772s |
| 22 | H | Ac | H | H | Ac | C | 3405(127) | 1674(823) 1656sh | 1529(90) | 1078(67) 1050(100) 1020(32) 988(49) 921(80) |
| | | | | | | N | 3250m | 1775w 1657sh 1644s | 1523m | 1259s 1241s 1066w 939m 891w 800m |
| 23 | H | *f* | H | H | $CO_2Me$ | N | 3250m | 1732, 1714 dbt s | 1537m | 1311m 1222s 1062m 1054m 1003m 970m 882m 824m 796m 763s 725w |
| | | | | | | | 3135w | 1657s | 1494w | |
| 24 | H | CHO | Et | Et | $CO_2Et$ | C | 3415(161) | 1688(482) 1650(700) | 1547(77) | 1114(207) 1089(189) 1062(77) 1015(136) 960(34) 922(27) |
| | | | | | | N | 3215m | 1688, 1663 dbt s | 1547m 1477w | 1256s 1133m 1024m 834m 756s |
| 25 | H | Me | CHO | $CO_2Et$ | Me | C | 3415(113) 3220(37) | 1677(596) 1658(512) | 1579(118) 1521(183) | 1288(151) 1259(193) 1170(489) 1089(386) 1028(51) |
| | | | | | | N | 3170w 3075m | 1701s 1655w 1634s | 1589m 1522m | 1327m 1289m 1268m 1174s 1084m 1014m 777m |
| 26 | H | Me | Ac | Me | $CO_2Et$ | C | 3430(136) 3245(36) | 1770(6) 1704sh 1678(430) 1650(515) | 1559(264) 1505(114) 1474(161) | 1101(230) 1062(203) 1018(79) 947(142) |
| | | | | | | N | 3235m | 1642s | 1554m 1513m | 1278s 1202s 1100m 1024m 942m 795m |
| 27 | H | Me | Ac | Et | $CO_2Et$ | C | 3430(127) 3250(29) | 1704sh 1680(429) 1652(586) | 1553(189) 1496(100) 1473sh | 1276(346) 1105(170) 1072(146) 1052(127) 1018(105) 951(103) |
| | | | | | | N | 3150m | 1703s 1625s | 1562m 1505m | 1286s 1271s 1185s 1096s 1070s 1051s 723w |
| 28 | H | Me | CHO | Me | $CO_2Et$ | C | 3415(115) 3240(28) | 1712sh 1666(930) | 1567(294) 1506(130) | 1253(509) 1095(183) 1019(74) 924(33) |
| | | | | | | N | 3240m | 1667s | 1561m 1513m | 1284s 1187m 1100m 1020m 793m 774m |
| 29 | H | CHO | Me | $CO_2Et$ | Me | C | 3415(93) 3210(53) | 1697(444) 1642, 1636 dbt (776) | 1565(107) 1488(187) | 1266(406) 1138(346) 1095(430) 882(40) 853(50) |
| | | | | | | N | 3205m | 1694m | 1560m | 1284s 1258s 1133s 1097s 887m 780m 768m 704m |
| 30 | H | $CO_2Me$ | $CO_2Et$ | Me | $CO_2Et$ | C | 3400(135) | 1708(1110) | 1563(168) 1492sh | 1284(665) 1069(406) 1015(137) 960(62) 854(62) |
| 31 | H | CHO | $CO_2Et$ | Me | $CO_2Et$ | C | 3400(116) | 1701(886) 1664(486) | 1553(142) 1489sh | 1123(145) 1071(464) 1013(96) 885(20) 858(49) |
| | | | | | | N | 3230m | 1709sh 1692s | 1552m | 1260s 1136m 1086m 1018m 863w, 785m 768m |
| 32 | H | $CO_2H$ | Et | Et | $CO_2Et$ | N | 3185m 2645m [g] | 1697w 1667s | 1552m | 1284s 1260s 1151s 1019m 916w 786m 770m |
| 33 | H | $CO_2H$ | Et | Et | $CO_2H$ | N | 3420m 2600m [g] | 1672sh 1650s | 1550m 1512w | 1272s 1192s 1061m 934m 788m |
| 34 | H | $CO_2H$ | Me | $CO_2Et$ | Me | N | 3240m 2654m [g] | 1695sh 1667s | 1554m 1507w | 1292s 1264s 1217m 1129m 1078m 916w 782m 725s |
| 35 | H | $CO_2Et$ | Me | $CO_2H$ | Me | N | 3225m 2605m [g] | 1656s (broad) | 1552m 1507sh | 1279s 1202s 1133m 1089s 1024m 928w 788m 780m 771m 736m |
| 36 | H | Me | CN | H | Me | C | 3425(77) 3245(47) 2229(250) [h] | — | 1600(46) 1515(31) | 1309(24) 1146(26) 1133(28) 1005(12) |
| 37 | H | Me | CN | CN | Me | C | 3405 3195 2237 [h] | — | 1600 1542 | Saturated solution |
| 38 | H | Me | CN | $CO_2Et$ | Me | C | 3405(65) 3205(75) 2234(198) [h] | 1697(549) | 1597(45) 1541(147) | 1284(300) 1139(366) 1095(308) 1015(41) |
| 39 | H | Me | CN | CHO | Me | N | 3160w 3115m 2220m [h] | 1637, 1623 dbt s | 1591m 1530m | 1096w 936m 817m 723w 683w |
| 40 | H | Me | CN | :NOH | Me | N | 3245sh 3145m 2220m [h] | 1626m (C=N) | 1586w 1522w | 1088w 965m 909s 780m 747m 723w |

[a] At 3488 in $CCl_4$. [b] Spectrum for liquid. [c] $CH_2{\cdot}N{<}[CH_2]_3$. [d] Substance A, di-(5-ethoxycarbonyl-3 : 4-dimethyl-2-pyrryl)methane. [e] Substance B, di-(5-ethoxycarbonyl-3-ethyl-4-methyl-2-pyrryl)methane. [f] $CO{\cdot}CO_2Me$. [g] OH band. [h] CN band. s = strong. m = medium. w = weak. sh = shoulder. dbt = doublet.

1500 cm.$^{-1}$. Pyrrole itself has absorption at 1575, 1561, and 1531 cm.$^{-1}$ which has been ascribed to the asymmetrical and symmetrical vibrations of the double bonds in the pyrrole ring.[15] These vibrations would be expected to depend considerably on the substitution of functional groups which would affect the symmetry of the molecule, and hence the position and intensity of these bands. Although there appears to be no empirical relation between the positions of the bands and the substitution on the pyrrole ring, it seems that the band near 1565 cm.$^{-1}$ is most intense when the functional substitution is at positions 2 : 4 or 3 : 4, and weakest in the 2 : 5-disubstituted pyrroles. This might be expected from a consideration of the symmetry of these vibrations.

Cromwell *et al.*[10] also found strong absorption in this region in αβ-unsaturated β-amino-ketones which was ascribed to a modified C=C or C–N stretching vibration similar to the amide II band. However, the absorption bands of the carbonyl-substituted pyrroles are of only weak or medium intensity and so the assignment to a ring vibration, similar to that in pyrrole itself, is preferred.

*Experimental.*—The spectra were recorded on a Grubb-Parsons D.B.I. double-beam infrared spectrometer with sodium chloride optics. Solid-state spectra were determined as paraffin mulls and solution spectra in chloroform using solutions of concentration about 0·5% w/v in a 0·5 mm. cell.

The preparation of the pyrroles was described in Part I. In addition, the pyrrole (4) was prepared as in ref. 16 and the pyrroles (6) and (27) as in ref. 17.

We are indebted to Professor C. Rimington, F.R.S., for a gift of pyrroles (19), (20), (21); to Dr. R. P. Linstead, C.B.E., F.R.S., for pyrroles (25) and (36—40); and to Dr. J. A. Elvidge for the compounds (11), (22), (23). The work was carried out with the financial support (to U. E.) from the Rockefeller Foundation to whom thanks are offered.

Imperial College of Science and Technology,
South Kensington, London, S.W.7.
Borough Polytechnic, Borough Road,
London, S.E.1.

[*Received, July 11th*, 1957.]

[15] Mirone, *Gazzetta*, 1956, **86**, 165.
[16] Eisner, Linstead, Parkes, and Stephen, *J.*, 1956, 1655.
[17] Eisner, Lichtarowicz, and Linstead, *J.*, 1957, 733.

---

## 196. *The Infrared Spectra of* N-*Heteroaromatic Systems. Part I. The Porphins.*

By S. F. Mason.

The infrared spectra of porphin, chlorin, and a number of their derivatives have been measured over the range 4000—400 cm.$^{-1}$. The spectra suggest that the porphin nucleus approximates to a symmetry $D_{4h}$ which is reduced to $V_h$ by the hydrogen atoms of the pyrrole N–H groups. The nitrogen atoms of the porphin nucleus are found to be extensively hydrogen-bonded, and it is shown, from a calculation of the overlap between the orbitals of a hydrogen atom and the four nitrogen atoms, that the bonding is responsible for the exceptionally low frequency of the in-plane N–H deformation vibration in porphin and chlorin. A number of bands characteristic of the porphin nucleus are listed and discussed.

The infrared spectra of a number of relatively complex natural and synthetic porphins have been reported.[1-4] A few assignments have been suggested for the vibrations of the porphin nucleus,[4] but attention has been concentrated mainly upon the characterisation

[1] Falk and Willis, *Austral. J. Sci. Res.*, 1951, **4**, 579.
[2] Craven, Reissmann, and Chinn, *Analyt. Chem.*, 1952, **24**, 1214.
[3] Vestling and Downing, *J. Amer. Chem. Soc.*, 1939, **61**, 3511.
[4] Thomas and Martell, *ibid.*, 1956, **78**, 1338.

TABLE 1. *The infrared spectra* (cm.$^{-1}$) *of porphin and its derivatives in the solid state. Values in parentheses refer to bands which appear, and values in italics to bands which disappear, or are considerably weakened, upon the replacement of the hydrogen atoms of the* N–H *groups by deuterium.* s = *strong*; m = *moderate*; w = *weak.*

(1) Porphin

| | |
|---|---|
| *3305m* | 1184m |
| 3181w | (1170w) |
| 3102m | *1158w* |
| 3036w | 1137m |
| 2997vw | (1098)w |
| 2954w | 1066w |
| 2921w | 1057m |
| 2851w | 1048m |
| 2782w | 1033w |
| 2742w | 995w |
| 2669w | *970s* |
| 2654w | 951s |
| 2597m | 901m |
| 2563vw | 853s |
| 2494vw | 841s |
| (2463w) | 809w |
| 2422vw | 792w |
| 2115vw | *771s* |
| 2100vw | (768s) |
| 1745vw | 749m |
| 1589w | 728s |
| 1406m | *719s* |
| 1352w | 690s |
| 1281w | 638m |
| 1262w | 618m |
| 1252w | (537w) |
| 1224m | |

(2) Copper porphin

| | |
|---|---|
| 3193w | 1388m |
| 3151w | 1357w |
| 3105w | 1310s |
| 3083m | 1246w |
| 3063w | 1192w |
| 3041w | 1153w |
| 3014w | 1115w |
| 2967w | 1060s |
| 2932w | 1036vw |
| 2888m | 1025w |
| 2832m | 996s |
| 2770vw | 901w |
| 2743w | 857s |
| 2681vw | 852s |
| 2690w | 802w |
| 2576w | 777w |
| 2423w | 768s |
| 2255w. | 744m |
| 2120w | 732w |
| 1985w | 700s |
| 1802w | 697s |
| 1531m | 618m |

(3) *æt*ioPorphin

| | |
|---|---|
| 3314m | 115s |
| 3100w | 1060s |
| 3052w | 987m |
| 3030w | 981w |
| 3009w | 956m |
| 2963s | 918w |
| 2930s | 902m |
| 2918s | 885w |
| 2867s | 837s |
| 1670w | 796w |
| 1459 | 760w |
| 1316w | 744s |
| 1270w | 730w |
| 1262w | 722w |
| 1239w | 708w |
| 1221m | 683s |
| 1192s | 648m |
| 1143m | 618m |

(4) Octaethylporphin

| | |
|---|---|
| 3310m | 1143w |
| 3114w | 1116s |
| 3092w | 1057s |
| 3052w | 1014s |
| 3030w | 1006m |
| 2967s | 974w |
| 2931s | 950s |
| 2869s | 893m |
| 2795w | 847w |
| 2750w | 834s |
| 2682w | 821m |
| 1611w | 795w |
| 1469m | 777w |
| 1377w | 745s |
| 1319m | 720m |
| 1279w | 699m |
| 1264w | 674m |
| 1240m | 643m |
| 1220m | 618m |
| 1188m | |

(5) Octamethylporphin

| | |
|---|---|
| 3311m | 906s |
| 2956w | 837s |
| 2912m | 783m |
| 2903m | 771m |
| 2850m | 734s |
| 2804w | 714m |
| 1400w | 692s |
| 1222m | 674w |
| 1195s | 647m |
| 1131m | 618m |
| 1111s | 605w |
| 935m | |

(6) Copper octamethylporphin

| | |
|---|---|
| 3188w | 1138w |
| 3115w | 1111w |
| 3025w | 1096m |
| 2962m | 940s |
| 2902s | 902w |
| 2850s | 838s |
| 1681m | 781s |
| 1390m | 725s |
| 1230s | 693w |
| 1202w | 607m |
| 1149s | 502w |

(7) Magnesium octamethylporphin

| | |
|---|---|
| 3109w | 1221m |
| 3095w | 1152s |
| 3030w | 1111w |
| 2956m | 1090w |
| 910s | 940m |
| 2850s | 932s |
| 2785w | 876w |
| 1458m | 834s |
| 1342w | 796w |
| 1319w | 779s |
| 1291w | 730s |
| 1270w | 695w |
| 1262w | 426w |
| 1230m | |

(8) *meso*-Tetramethylporphin

| | |
|---|---|
| 3322m | 1025w |
| 3114w | 962m |
| 3094w | 954s |
| 2916s | 914s |
| 2850s | 895w |
| 1474m | 880w |
| 1430w | 776s,b |
| 1406w | 743w |
| 1354m | 709s |
| 1240m | 692 |
| 1204w | 643m |
| 1172s | 624m |
| 1122s | 592w |

(9) Copper *meso*-tetramethylporphin

| | |
|---|---|
| 3114m | 1119w |
| 3008w | 1089s |
| 2915s | 1069s |
| 2854s | 1030w |
| 2796w | 982s |
| 2759m | 925s |
| 2572w | 892m |
| 1526m | 792w |
| 1451m | 776s |
| 1361w | 730w |
| 1342s | 700s |
| 1305m | 675m |
| 1258s | 649w |
| 1164w | 611m |
| 1147w | |

(10) *meso*-Tetraphenylporphin

| | |
|---|---|
| *3311m* | 1072m |
| 3118w | 1057w |
| 3076w | 1031m |
| 3050m | 1002s |
| 3026m | *980m* |
| 2958w | 966s |
| 2915w | 920w |
| 2851w | 901w |
| 2705w | 876m |
| 2592w | 851m |
| (2478w) | 830w |
| 1596m | 814m |
| 1470m | 795s |
| 1440m | 787s |
| 1353m | (773w) |
| 1287w | 760m |
| 1271w | 749m |
| 1250m | 730m |
| 1221m | *725m* |
| 1212m | 706m |
| 1186m | 699s |
| 1170m | 655s |
| 1153m | 638m |
| 1113w | 620m |
| (1097w) | 563w |
| 1080w | 512m |

(11) Copper *meso*-tetraphenylporphin

| | |
|---|---|
| 3120w | 1076m |
| 3070w | 1006s |
| 3049m | 997m |
| 3014m | 990m |
| 2916m | 876w |
| 2850w | 838w |
| 1598m | 800s |
| 1449m | 763w |
| 1349m | 752m |
| 1208w | 740w |
| 1180w | 721m |
| 1158w | 700m |
| 1113w | 644m |
| 1087w | 620w |

(12) Chlorin

| | |
|---|---|
| 3348m | 1064w |
| 3118m | 1050m |
| 3095m | 1037s |
| 3076w | 1005w |
| 2957m | 982m |
| 2928m | 965s |
| 2886w | 958s |
| 2732w | 946s |
| 2630w | 906w |
| 2534w | 857s |
| 1618s | 840s |
| 1594m | 796m |
| 1464m | 784m |
| 1397m | 776s |
| 1307m | 770s |
| 1254m | 742w |
| 1230w | 720w |
| 1218m | 706s |
| 1190w | 696s |
| 1166s | 643m |
| 1142s | 620w |

(13) Copper chlorin

| | |
|---|---|
| 2918m | 1005m |
| 2855w | 993s |
| 1612m | 976m |
| 1339w | 876m |
| 1262m | 860s |
| 1214s | 839s |
| 1180s | 769w |
| 1152m | 745w |
| 1114w | 425w |
| 1058s | |

XUM

TABLE 1. (*Continued.*)

| (14) *meso*-Tetramethylchlorin | | (16) Copper octamethylch orin (*contd.*) | | (18) Copper octaethylchlorin (*contd.*) | | (20) Tetra-azaporphin (*contd.*) | |
|---|---|---|---|---|---|---|---|
| 3342m | 1080m | 1648m | 870w | 1453m | 916m | 1286w | 696m |
| 3120w | 1063s | 1596m | 850m | 1390w | 850s | 1270w | 638m |
| 3025w | 1030w | 1400m | 821s | 1367w | 833s | 1261w | 620w |
| 3002w | 1018w | 1310m | 779w | 1312m | 811m | 1243m | |
| 2988w | 968m | 1278w | 768w | 1268m | 746s | | |
| 2918s | 954s | 1246m | 748m | 1225w | 726s | (21) Octamethyltetra-azaporphin | |
| 2860s | 940s | 1213s | 727s | 1198s | 700m | | |
| 2716w | 925m | 1196m | 690m | 1189s | 620m | 3299m | 1143s |
| 2560w | 916w | 1152s | 620m | 1145m | | 3030w | 1104s |
| 2494w | 876m | | | | | 2938w | 1017m |
| 1975w | 837w | (17) Octaethylchlorin | | (19) Octaethyltetrahydroporphin | | 2912m | 935m |
| 1591s | 771s, b | | | | | 2848m | 887s |
| 1471s | 748m | *3338m* | *1014m* | 3351m | 1129w | 2745w | 779ms |
| 1360s | 714s, b | 3095w | (1010m) | 3100w | 1111m | 2666w | 769s |
| 1312m | 698s | 3049w | 996s | 3072w | 1062m | 2623w | 756s |
| 1286w | 681m | 3030w | 974w | 2950s | 1057w | 2533w | 735m |
| 1268w | 636m | 3014w | 948s | 2917s | 1007s | 2210w | 709m |
| 1249m | 618w | 2960s | 905s | 2856s | 946m | 1985w | 695s |
| 1237s | 598m | 2930s | 872w | 1641w | 866m | 1484s | 652m |
| 1148w | 572w | 2917s | 849m | 1598s | 828m | 1421m | 621w |
| 1116m | | 2886m | 826m | 1445m | 788w | 1408w | 600m |
| | | 2869s | *820m* | 1385w | 776s | 1262m | 559w |
| (15) Octamethylchlorin | | 2855m | (817m) | 1318w | 725w | 1230w | 490s |
| | | (2491m) | *812m* | 1287w | 721w | 1202w | 471w |
| 3340m | 1090m | 1614m | 797w | 1272w | 682w | 1151s | |
| 2958m | 1076w | 1458m | 773w | 1239w | 638m | | |
| 2908s | 1039m | 1400m | 754w | 1182s | | (22) Tetrahydro-octamethyltetra-azaporphin | |
| 2853m | 943m | 1319w | 738m | | | | |
| 1611s | 932w | 1300w | 731m | | | 3332m | 941w |
| 1522w | 917m | 1273w | *717m* | (20) Tetra-azaporphin | | 2968m | 927w |
| 1450w | 898s | 1261w | (703w) | | | 2911s | 915w |
| 1400w | 845m | 1233m | *695m* | 3296m | 1226m | 2868s | 876s |
| 1275w | 824m | 1208w | (682w) | 3120w | 1183m | 2844s | 811w |
| 1247w | 779w | 1191m | 645m | 3090m | 1134w | 2732w | 787w |
| 1230w | 766s | 1169s | 618m | 3076m | 1109w | 1558s | 773m |
| 1203s | 710m | *1145w* | (590w) | 3029w | 1057w | 1492s | 757w |
| 1165s | 688s | *1110m* | (512w) | 3008w | 1044m | 1410w | 746s |
| 1144m | 650m | 1059s | | 2922w | 980w | 1379s | 725m |
| 1127w | 618w | | | 2850w | 963w | 1354m | 716w |
| 1113m | 590m | (18) Copper octaethylchlorin | | 2130w | 937s | 1296s | 701m |
| | | | | 2060vw | 928s | 1262w | 691s |
| (16) Copper octamethylchlorin | | | | 2010vw | 876w | 1224w | 674s |
| | | 3100w | 1129m | 1990vw | 829s | 1164m | 653m |
| 3042w | 1146m | 3070w | 1112m | 1647m | 792s | 1140s | 618w |
| 3027w | 1129m | 2949s | 1061s | 1619s | 762m | 1110s | 591m |
| 3009w | 1111w | 2917s | 1057s | 1507m | 740m | 1061m | 490s |
| 2961m | 1069w | 2838m | 1016s | 1480m | 738m | 1040m | 467w |
| 2904s | 981w | 1629m | 988s | 1428w | 723m | 1007s | |
| 2850s | 925s | 1573m | 957s | 1357w | 715s | | |

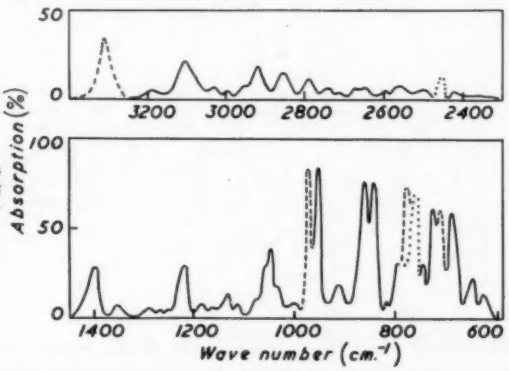
of substituent groups [1,2,4] and the position of the N–H stretching frequency.[1,3,4] In the present work a study has been made of the spectra of porphin and chlorin, the parent nuclei of the porphyrin and the chlorophyll series respectively, and of a range of their simpler and more symmetrical derivatives, including the metal complexes. The frequencies and approximate intensities of the infrared absorption bands of porphin, chlorin, and their derivatives in potassium bromide discs over the range 4000—400 cm.$^{-1}$ are listed in Table 1.

The crystallographic evidence for phthalocyanine [5] suggests that the porphin nucleus approximates to $D_{4h}$ symmetry, but belongs, more precisely, to the point group $V_h$ (two two-fold axes in the plane through opposite *meso*-positions), owing to hydrogen bonding between the pyrrolic nitrogen atoms; [5] a conjugation distortion of the nuclear framework may also contribute to this as nickel phthalocyanine deviates slightly, though less than the parent molecule, from $D_{4h}$ symmetry.[6] Thus the infrared spectrum of porphin should

[5] Robertson, *J.*, 1936, 1195.
[6] Robertson and Woodward, *J.*, 1937, 221.

consist of a few strong bands, those allowed according to the selection rules of the $D_{4h}$ group, and a large number of weak bands, due in part to forbidden frequencies which become allowed in combination with each other, and in part to frequencies which become allowed upon the reduction of the $D_{4h}$ symmetry. The infrared spectrum of porphin is found to be of this character (Fig. 1, Table 1). However, the N–H vibrations should obey the selection rules of the actual point group to which the porphin molecule belongs, as the central hydrogen atoms are the main source of the reduction of the $D_{4h}$ symmetry. If these hydrogen atoms are located on adjacent pyrrolic nitrogen atoms (cf. I), the symmetry is reduced to $C_{2v}$ and five N–H vibrations are allowed; but if they are placed on opposite nitrogen atoms (cf. II) or symmetrically hydrogen-bond a pair of nitrogen atoms each (cf. III) the symmetry is lowered only to $V_h'$ or $V_h$ (two two-fold axes in the plane through the nitrogen atoms or through the *meso*-positions respectively) and only three N–H vibrations are allowed. By replacing the central hydrogen atoms with deuterium

FIG. 1. *The infrared spectrum of porphin.*



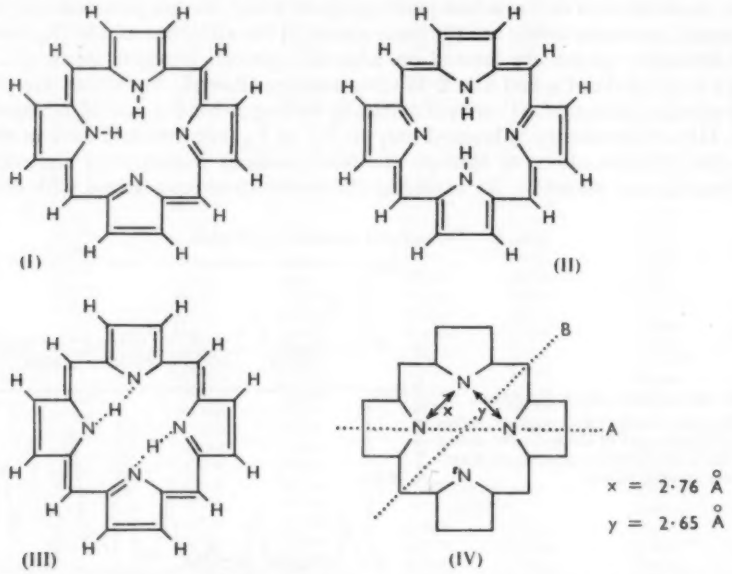

--- *The main bands which disappear.*
. . . *The main bands which appear, upon the replacement of the hydrogen atoms of the* N–H *groups by deuterium (potassium bromide discs).*

the N–H vibrations may be identified, the frequencies obtained being listed in Table 2. From the masses of the nitrogen, hydrogen, and deuterium atoms, and from the analogous case of pyrrole,[7] the frequencies of a given N–H vibration in deuterated and undeuterated porphin should have the ratio of about 1·35 for stretching vibrations and 1·1—1·3 for bending vibrations. Taking pairs of bands, one of which appears and the other disappears on deuteration, it is found (Table 2) that not more than three N–H vibrations are allowed in the porphins studied, whilst five are allowed in the case of octa-ethylchlorin, which cannot have a higher symmetry than $C_{2v}$. Of the five N–H vibrations of octa-ethylchlorin, only one lies in the N–H stretching-vibration region and, as only three N–H bending modes are allowed in the $C_{2v}$ point group, the symmetry of this molecule is probably $C_s$.

The N–H stretching vibration of porphin and octaethylchlorin shifts only a few cm.$^{-1}$ to higher frequencies when one passes from the solid state to carbon tetrachloride solution, and the corresponding vibration of pyrrole in solution is some 150—200 cm.$^{-1}$ higher in frequency (Tables 1 and 2). Thus there is considerable hydrogen-bonding in porphins and chlorins, and it must be almost entirely intramolecular, even in the solid state. However, the bonding is of an unusual nature, as for porphin the in-plane N–H deformation vibration lies at a lower frequency than that for pyrrole by 170 or 420 cm.$^{-1}$ (Table 2), whilst in amides [8] and aromatic amines [9] hydrogen-bonding has the effect of raising the in-plane deformation frequency, as the bonding is favoured by a linear arrangement of the N–H · · · X system.

[7] Lord and Miller, *J. Chem. Phys.*, 1942, **10**, 328.
[8] Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen, London, 1954.
[9] Unpublished result of the author.

The unusual character of the hydrogen-bonding in porphin may be accounted for by a calculation of the overlap between the 1*s* orbital of a hydrogen atom and the hybrid 2*s*2*p* orbitals of the nitrogen atoms within the rectangular area bounded by the four pyrrolic nitrogen atoms of the porphin nucleus (Fig. 2). The crystal structure of phthalocyanine [5]




shows that the C–N–C bond angles of the pyrrole rings are almost tetrahedral (108·5°) so that the bonds from nitrogen to carbon may be taken to be nearly $sp^3$ hybrids. The third nitrogen orbital is purely $2p\pi$, and so the fourth, directed towards the centre of the porphin molecule, is nearly digonal, *sp*. The fourth orbital is occupied by lone-pair electrons in

TABLE 2. *Infrared frequencies (cm.$^{-1}$) of the* N–H *vibrations of pyrrole and of porphin and its derivatives in the condensed state and in carbon tetrachloride solution.*

| Compound | Vibration | N–H | | N–D |
|---|---|---|---|---|
| | | Solution | Condensed state | Condensed state |
| Pyrrole | stretch | 3497 [a] | 3400 [b] | 2525 [b] |
| | i.p. deformation | | 1146 [b] | 915 [b] |
| | o.p. deformation | | 565 [b] | 450 [b] |
| Porphin | stretch | 3309 | 3305 | 2463 |
| | deformation | | 970 | 768 |
| | " | | 719 | 537 |
| *meso*-Tetraphenylporphin | stretch | 3315 | 3311 | 2478 |
| | deformation | | 980 | 773 |
| | " | | 725 | |
| Octaethylchlorin | stretch | 3343 | 3338 | 2491 |
| | deformation | | 1014 | 817 |
| | " | | 820 | 703 |
| | " | | 812 | 682 |
| | " | | 717 | 590 |

[a] Fuson, Josien, Powell, and Utterback, *J. Chem. Phys.*, 1952, **20**, 145. [b] Lord and Miller, *ibid.*, 1942, **10**, 328.

the case of two of the four pyrrolic nitrogen atoms, and this factor also favours the assumption of a large " *s* " character in the orbitals directed towards the centre of the nucleus. Taking the dimensions of porphin (IV) to be the same as those of the azaporphin

nuclear framework of phthalocyanine,[5] it is found, by using Slater orbitals,[10] that the overlap of the digonal hybrid orbitals of four nitrogen atoms and a 1s orbital of a hydrogen atom is considerable everywhere in the rectangle bounded by the nitrogen atoms (Fig. 2). In particular, the overlap is approximately unity round the perimeter of a circle with a radius of 0·9 Å from the centre of the molecule, and the overlap along an axis through opposite nitrogen atoms (Fig. 2*A*) up to this distance, which corresponds to a N–H bond length of 1·0 Å, is not appreciably greater than the overlap along an axis through opposite *meso*-positions (Fig. 2*B*). Overlap affords a measure of bond strength,[11] and the present calculations suggest that the $V_h$ models of porphin (II and III) are about equally stable, whilst the $C_{2v}$ model (I) is less stable, owing to the greater penetration of each hydrogen atom into the van der Waals sphere of the other. The overlap calculations also indicate that in-plane deformation of a N–H bond in porphin occurs more readily, and the out-of-plane deformation less readily, than in the case of pyrrole, a consequence which is supported by the

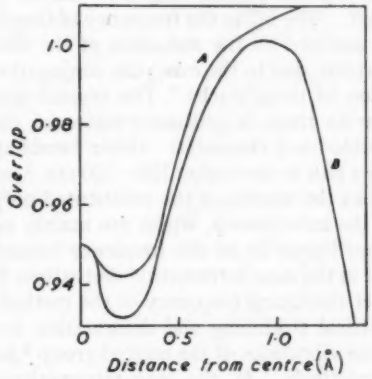



FIG. 2. *The overlap of the sp hybrid orbitals of the four nitrogen atoms directed towards the centre of the porphin molecule and the* 1s *orbital of a hydrogen atom as a function of the distance of the hydrogen atom from the centre of the molecule; (A) along an axis through opposite nitrogen atoms; and (B) along an axis through opposite* meso*-positions [axes (A) and (B) respectively of* (IV)].

frequencies of the absorptions due to these vibration modes (Table 2). On reduction to chlorin, and then to tetrahydroporphin, the porphin ring system is progressively expanded, the overlap of the nitrogen and hydrogen orbitals being reduced. Accordingly, the in-plane vibrations of the N–H group should increase in frequency in the series tetrahydroporphin > chlorin > porphin, as is found (Tables 1 and 2).

Other absorption bands of porphin which should be indicative of the structure of the molecule are those due to the out-of-plane C–H deformation vibrations. The absorptions due to these modes in aromatic systems are quite strong,[12] and they have been well characterised.[13] Two out-of-plane C–H vibrations should absorb radiation in the $D_{4h}$ model of porphin, three in the $V_h'$ model (II), four in the $V_h$ model (III), and seven in the $C_{2v}$ model (I). In the $D_{4h}$ point group, the C–H groups of the set of pyrrolic positions and those of the set of *meso*-positions must move in phase, but the two sets may be either in or out of phase with each other, for the allowed infrared transitions (symmetry $A_{2u}$). The two resultant absorption bands probably lie in the range 830—880 cm.$^{-1}$ in the porphins, since of two fairly strong bands in this range one, between 834 and 852 cm.$^{-1}$, disappears on *meso*-substitution, and the other, between 853 and 876 cm.$^{-1}$, is absent from the spectra of the compounds substituted in the pyrrolic positions (Table 1). Other bands due to out-of-plane C–H vibrations, if present, are either too weak or vary too widely in frequency from compound to compound to be identified. Six transitions due to in-plane C–H vibrations are allowed according to the $D_{4h}$ model of porphin. The bands at 1048, 1184,

[10] Mulliken, Rieke, Orloff, and Orloff, *J. Chem. Phys.*, 1949, **17**, 1248.
[11] Coulson, "Valence," Oxford Univ. Press, 1952.
[12] Spedding and Whiffen, *Proc. Roy. Soc.*, 1956, *A*, **238**, 245.
[13] Whiffen, *Spectrochim. Acta*, 1955, **7**, 253; *J.*, 1956, 1350.

and 1224 cm.$^{-1}$ in the spectrum of porphin may be due to the allowed in-plane deformation modes, and those at 3036, 3102, and 3181 cm.$^{-1}$ to the allowed stretching modes.

A number of bands, due to ring vibrations, appear consistently in the spectra of the majority of the compounds studied. Bands near 620, 690, 770, and 1110 cm.$^{-1}$ are particularly insensitive to substitution in the porphin nucleus and to reduction of the nucleus to the di- and the tetra-hydro-stage, suggesting that these bands are due to the vibrations of moities common to the whole series of compounds, namely, the pyrrole rings. The ring breathing vibration of pyrrole lies [7] at 1144 cm.$^{-1}$, and the 1110 cm.$^{-1}$ band of the porphins may be due to a corresponding vibration in which opposite pyrrole rings undergo the breathing motion out of phase (symmetry $E_u$ in $D_{4h}$). The 620 and 690 cm.$^{-1}$ bands of the porphins may be due to similar $E_u$ out-of-phase combinations of in-plane pyrrole ring deformation vibrations which absorb at 647 and 711 cm.$^{-1}$ respectively in pyrrole,[7] and the 770 cm.$^{-1}$ band of the porphins to an in-phase combination (symmetry $A_{2u}$ in $D_{4h}$) of an out-of-plane pyrrole ring deformation vibration which absorbs [7] at 838 cm.$^{-1}$ in pyrrole itself. The fall in the frequency of these vibrations on passage from pyrrole to porphin may be ascribed to the reduction of the double-bond character of the pyrrole ring bonds in porphin, due to the exocyclic conjugation of the pyrrole nuclei, permitting readier deformation of those nuclei. The crystallographic evidence shows [5] that the αβ-bonds of the pyrrole rings in phthalocyanine are particularly long (1·49 Å), and so possess a small double-bond character. Other bands appearing regularly in the spectra of the porphins are a pair in the region 725—750 cm.$^{-1}$, and one in the range 950—1000 cm.$^{-1}$ (Table 1).

In the spectra of the substituted porphins there are a number of absorption bands due to the substituents, which are mainly either methyl or ethyl groups. For the most part these bands lie in the frequency ranges characteristic of the vibrations of such groups, but in the *meso*-tetramethyl derivatives (compounds 8, 9, and 14, Table 1) the asymmetrical C–H stretching frequency of the methyl groups is lowered by some 40 cm.$^{-1}$ and the symmetrical stretching and deformation frequencies by some 20 cm.$^{-1}$, the usual ranges for these vibrations of the methyl group [8] being 2962 ± 10, 2872 ± 10, and 1380—1370 cm.$^{-1}$ respectively. In the *meso*-tetramethylporphins there is steric hindrance between each methyl group and the β-C–H groups of the two adjacent pyrrole rings, and the resultant compression lowers the effective restoring force, and thus the frequencies, of these vibrations of the methyl group.

## Experimental

*Materials.* The compounds used in the present investigation were kindly supplied by Dr. U. Eisner,[14] Professor C. Rimington kindly providing an additional specimen of porphin. The porphin derivatives listed in Table 2 were deuterated by three successive equilibrations in dioxan–deuterium oxide.

*Infrared spectra.* These were measured with a Perkin-Elmer model 12 C spectrometer, prisms of lithium fluoride, sodium chloride, and potassium bromide being used for the ranges 4000—2000, 2000—700, and 700—400 cm.$^{-1}$ respectively. The compounds were examined as solids included in pressed potassium bromide discs, which, contrary to previous experience,[4] gave better spectra than suspensions in mulling agents. The compounds listed in Table 2 were also examined in carbon tetrachloride solution.

The author is indebted to Dr. U. Eisner and Professor C. Rimington for the provision of compounds, and to the Australian National University for a Research Fellowship.

Australian National University.
Chemistry Department, The University, Exeter. [*Received, October 7th*, 1957.]

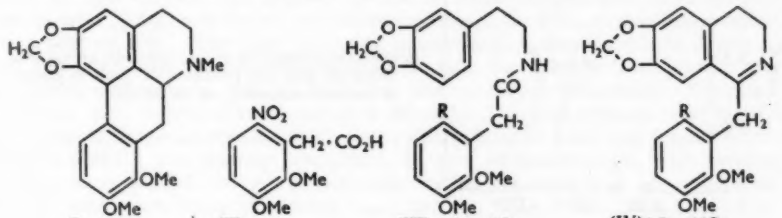
[14] Eisner, *J.*, 1957, 854, and references cited therein.

## 197. *Synthesis of* (±)-*Crebanine.*

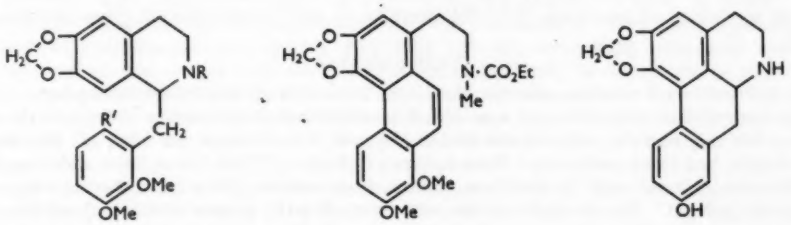
By T. R. Govindachari, K. Nagarajan, and C. V. Ramadas.

The synthesis of (±)-crebanine is reported.

The alkaloid, crebanine, $C_{20}H_{21}O_4N$, isolated by Japanese workers from *Stephania sasakii* and *S. capitata*, has been assigned structure (I) on the basis of degradative studies.[1] Manske,[2] considered that the methoxy-groups were in positions not accountable for by known biosynthetic routes and that the structure should be accepted with reserve. However, this structure has now been established by synthesis.



(I) (II) (III): R = $NO_2$ (IIIa): R = H (IV): R = $NO_2$ (IVa): R = H



(V): R = Me, R′ = $NH_2$ (Va): R = R′ = H (Vb): R = Me, R′ = H (VI) (VII)

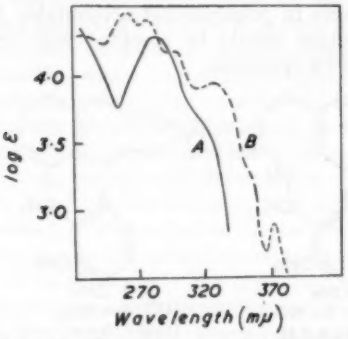
2 : 3-Dimethoxy-6-nitrophenylacetic acid (II) was obtained from 2 : 3-dimethoxy-6-nitrobenzaldehyde, through the benzyl alcohol, chloride, and nitrile, and condensed with homopiperonylamine to yield the amide (III). Cyclisation with phosphorus pentachloride in chloroform gave the dihydro*iso*quinoline (IV) which, by reduction of its methiodide, furnished 1-(6-amino-2 : 3-dimethoxybenzyl)-1 : 2 : 3 : 4-tetrahydro-2-methyl-6 : 7-methylenedioxy*iso*quinoline (V). Pschorr reaction of this base gave a product isolated as the hydriodide, m. p. 250° (decomp.), from which the free base, m. p. 123—123·5°, was obtained and identified, as indicated below, as (±)-crebanine. The ultraviolet spectra of both the hydriodide and the base (see Figure) showed only one maximum (at 280 mμ), whereas aporphines generally exhibit two maxima (near 275 and 300 mμ). The possibility of the Pschorr product's being a mere tetrahydro*iso*quinoline derivative, arising from (V) by deamination, alone or with simultaneous *N*-dealkylation,[3] was therefore considered. The tetrahydro*iso*quinoline derivatives (Va and b) were synthesised from the amide (IIIa) through the dihydro*iso*quinoline (IVa), reduction of which furnished the base (Va); the

[1] Tomita, *J. Pharm. Soc. Japan*, 1939, **59**, 207; Tomita and Shirai, *ibid.*, 1942, **62**, 27; 1943, **63**, 233; Shirai, *ibid.*, 1942, **62**, 517.

[2] Manske, "The Alkaloids, Chemistry and Physiology," Part IV, Academic Press Inc., New York, 1954, p. 129.

[3] Hey and Turpin, *Chem. and Ind.*, 1954, 216; *J.*, 1954, 2471; Govindachari and Arumugam, *J. Sci. Ind. Res., India*, 1955, **14**, *B*, 250.

methiodide of the dihydro-compound (IVa) gave the corresponding 2-methyl compound (Vb). Neither of the two was however identical with the hydriodide, m. p. 250° (decomp.), obtained in the Pschorr reaction. The ultraviolet absorption spectrum of the base, m. p. 123—123·5°, was superposable on that of natural crebanine, kindly provided by Professor Tomita. Treatment of either the synthetic or the natural base with ethyl chloroformate yielded the same compound (VI) (m. p. and mixed m. p.), with the expected spectrum




*Ultraviolet absorption of (A) synthetic or natural crebanine and (B) product* (VI) *from synthetic or natural crebanine, all in* EtOH.

(see Figure). The structure (I) for crebanine is thus established. It is possible that nuclear oxidation of anolobine (VII) followed by *O*- and *N*-methylation gives crebanine.

## Experimental

**2 : 3-*Dimethoxy-6-nitrophenylacetic Acid*.**—2 : 3-Dimethoxy-6-nitrobenzaldehyde [4] (18 g.) in dry *iso*propyl alcohol (150 ml.) was added to aluminium *iso*propoxide (4·5 g.) in the same solvent (50 ml.), and the solution distilled at the rate of 2—3 drops per min., till 90—100 ml. of distillate had been collected. More *iso*propyl alcohol (70 ml.) was then added and the distillation continued until the distillate was free from acetone (10 hr.) and then to remove the remaining solvent. The cooled residue was treated with concentrated hydrochloric acid (20 ml.) in water (150 ml.), to give 2 : 3-dimethoxy-6-nitrobenzyl alcohol (16 g.), pale yellow needles (from alcohol), m. p. 91—91·5°. The alcohol (10 g.) was added slowly to thionyl chloride (20 ml.) at 0°. When the initial vigorous reaction had ceased, the solution was boiled under reflux for ½ hr., cooled, and poured on ice (200 g.) to yield an oil which solidified to give 2 : 3-dimethoxy-6-nitrobenzyl chloride (12 g.), forming white crystals [from benzene–light petroleum (b. p. 40—60°)], m. p. 132°. The crude benzyl chloride (10 g.) was converted into the cyanide by refluxing it with potassium cyanide (18 g.) in water (18 ml.) and alcohol (160 ml.). The cyanide (5 g.) was converted [5] into the imidoate by saturating its methanol solution (6 ml.) with hydrogen chloride, and thence by hydrolysis into 2 : 3-*dimethoxy-6-nitrophenylacetic acid* (2 g.), needles (from benzene), m. p. 181·5° (Found: C, 50·3; H, 4·4. $C_{10}H_{11}O_6N$ requires C, 49·8; H, 4·6%).

**N-(2 : 3-*Dimethoxy-6-nitrophenylacetyl*)-3 : 4-*methylenedioxyphenethylamine*.**—The foregoing acid (0·5 g.) in chloroform (7 ml.) was warmed with thionyl chloride (2 ml.) at 40° for 2 hr. and the solvents then removed at 30° *in vacuo*. The residue was taken up in benzene (15 ml.) and added with stirring to homopiperonylamine (0·5 g.) in benzene (5 ml.), and the mixture made alkaline after some time and left at 0° overnight, to give the colourless *amide* (0·8 g.), m. p. 195° (from alcohol) (Found: C, 58·7; H, 5·2. $C_{19}H_{20}O_7N_2$ requires C, 58·8; H, 5·2%).

**1-(2 : 3-*Dimethoxy-6-nitrobenzyl*)-3 : 4-*dihydro-6* : 7-*methylenedioxyisoquinoline*.**—The foregoing amide (0·5 g.) in chloroform (7 ml.) was left with phosphorus pentachloride (0·8 g.) for 72 hr. The chloroform was then removed *in vacuo* and the residue extracted with hot water and filtered. Addition of concentrated aqueous ammonia precipitated the iso*quinoline* (0·15 g.), m. p. 169° (from methanol) (Found: C, 61·4; H, 5·0. $C_{19}H_{16}O_6N_2$ requires C, 61·6; H, 4·9%). The yellow *methiodide*, prepared by methyl iodide in hot chloroform, separated from alcohol and had m. p. 192° (decomp.) (Found: C, 47·1; H, 4·3. $C_{20}H_{21}O_6N_2I$ requires C, 46·9; H, 4·1%).

[4] Perkin, Robinson, and Stoyle, *J.*, 1924, **125**, 2358.
[5] Kay and Pictet, *J.*, 1913, **103**, 947.

1-(6-*Amino*-2 : 3-*dimethoxybenzyl*)-1 : 2 : 3 : 4-*tetrahydro*-2-*methyl*-6 : 7-*methylenedioxy*isoquinoline.—The above methiodide (1·7 g.) in methanol (65 ml.) containing Adams catalyst (0·15 g.) was shaken with hydrogen at 56 lb./sq. in. for 2 hr. The solution was filtered from the catalyst and evaporated. The residue was triturated with dilute sodium hydroxide solution and extracted with ether. The dried ($K_2CO_3$) ether extract was treated with hydrogen chloride, and the gummy precipitate triturated with alcohol, to give a *dihydrochloride* (0·65 g.), which, after recrystallisation from alcohol–ether, had m. p. 224° (decomp.) (Found: C, 54·9; H, 6·6. $C_{20}H_{26}O_4N_2Cl_2,\frac{1}{2}H_2O$ requires C, 54·8; H, 6·2%).

(±)-*Crebanine*.—The above dihydrochloride (0·6 g.) in 2N-sulphuric acid (10 ml.) and methanol (10 ml.) was treated at 0°, with stirring, with sodium nitrite (0·15 g.) in water (2 ml.). After 1 hr. the solution was allowed to rise to room temperature. Freshly precipitated copper powder (0·2 g.) was added and stirring continued for ½ hr. at that temperature and for another ½ hr. at 100°. Zinc dust (1 g.) and concentrated hydrochloric acid (2 ml.) were then added and after being heated and stirred for 20 min. the mixture was filtered. The filtrate was basified with aqueous sodium hydroxide and extracted with ether. The ether extract was shaken with N-hydrochloric acid (3 × 20 ml.). The acid extracts were neutralised by solid sodium hydrogen carbonate, made just acidic with acetic acid, and treated with excess of potassium iodide. The gummy precipitate, on two recrystallisations from methanol, gave (±)-*crebanine hydriodide* (0·1 g.), as colourless needles becoming pink on storage, m. p. 250° (decomp.) with preliminary blackening, $\lambda_{max.}$ 280 mμ (log ε 4·38) (Found: C, 51·2; H, 4·8. $C_{20}H_{22}O_4NI$ requires C, 51·4; H, 4·7%), yielding, by basification and ether-extraction, (±)-*crebanine*, stout needles [from light petroleum (b. p. 40—60°)], m. p. 123—123·5°, $\lambda_{max.}$ 280 mμ (log ε 4·29) (Found: C, 70·8; H, 6·3. $C_{20}H_{21}O_4N$ requires C, 70·8; H, 6·2%).

8-(2-N-*Ethoxycarbonyl*-N-*methylaminoethyl*)-1 : 2-*dimethoxy*-5 : 6-*methylenedioxyphenanthrene*.—(±)-Crebanine (80 mg.) in chloroform (10 ml.) containing potassium hydroxide (60 mg.) and ice was shaken with ethyl chloroformate (0·07 ml.) in chloroform (3 ml.). After 1 hr., more potassium hydroxide and ethyl chloroformate were added. Next day the chloroform solution was separated, washed with water, dilute acid, and water, dried ($Na_2SO_4$), and evaporated, to yield the *phenanthrene* (70 mg.), slender needles with a violet tint [from ether–light petroleum (b. p. 40—60°)], m. p. 125°, undepressed by a specimen (7 mg.), m. p. 125°, obtained by the same procedure from natural crebanine (10 mg.); this had $\lambda_{max.}$ 260, 275, 295, 325, 370 mμ (log ε 4·46, 4·40, 4·17, 3·93, 2·87) (Found: C, 67·5; H, 6·5. $C_{22}H_{25}O_4N$ requires C, 67·2; H, 6·1%).

N-(2 : 3-*Dimethoxyphenylacetyl*)-3 : 4-*methylenedioxyphenethylamine*.—*o*-Homoveratric acid (2 g.) was converted into the chloride and treated with homopiperonylamine, yielding the *amide* (2·5 g.), colourless needles (from methanol), m. p. 100—101° (Found: C, 66·1; H, 6·3. $C_{19}H_{21}O_5N$ requires C, 66·5; H, 6·1%).

1-(2 : 3-*Dimethoxybenzyl*)-1 : 2 : 3 : 4-*tetrahydro*-6 : 7-*methylenedioxy*isoquinoline.—The above amide (1 g.) in toluene (15 ml.) was refluxed with phosphoryl chloride (4 ml.) for 2 hr. and the whole poured on ice. The yellow solution was shaken with ether to remove toluene and non-basic material, then cooled and basified with aqueous sodium hydroxide. The liberated dihydro*iso*quinoline was taken up in ether, and the dried ($K_2CO_3$) ether extract saturated with hydrogen chloride, to give the hygroscopic hydrochloride (0·5 g.). This was reduced in alcohol (20 ml.) by Adams catalyst (0·15 g.). The solution was filtered and evaporated. An aqueous solution of the residue was treated with excess of potassium iodide, and the precipitate recrystallised from alcohol–ether, to give the *tetrahydroisoquinoline hydriodide* as needles, m. p. 196—197° (Found: C, 50·4; H, 5·0. $C_{19}H_{22}O_4NI$ requires C, 50·1; H, 4·8%).

1-(2 : 3-*Dimethoxybenzyl*)-1 : 2 : 3 : 4-*tetrahydro*-2-*methyl*-6 : 7-*methylenedioxy*isoquinoline.—The crude dihydro*iso*quinoline base from cyclisation of the amide (2 g.) was converted into the gummy methiodide by methyl iodide in chloroform. Reduction of the methiodide (0·35 g.) in methanol (20 ml.) with Adams catalyst (0·15 g.) during 2 hr. gave, after filtration, evaporation, and crystallisation of the residue from alcohol–ether, the *tetrahydro*-2-*methylisoquinoline hydriodide* (0·2 g.), m. p. 175—176° (Found: C, 51·2; H, 5·4. $C_{20}H_{24}O_4NI$ requires C, 51·2; H, 5·1%).

We are grateful to Professor M. Tomita for a gift of natural crebanine and to Mr. S. Selvavinayagam for microanalyses.

PRESIDENCY COLLEGE, MADRAS. [*Received, August 26th*, 1957.]

XUM

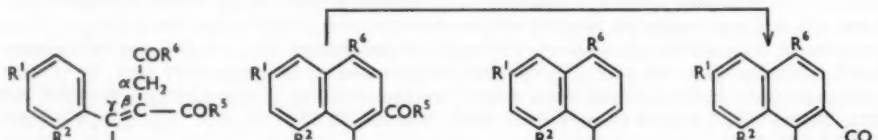
## 198. 1-*Phenylnaphthalenes. Part IV.* The Cyclisation of Methyl Hydrogen* cis- *and* trans-γ-o-*Methoxyphenyl- and Ethyl Hydrogen* cis- *and* trans-γ-p-*Methoxyphenyl-γ-phenylitaconate to the Corresponding* 1-*Phenylnaphthalenes.*

By F. G. Baddar, Lanson S. El-Assal, and (Mrs.) Victorine B. Baghos.

β-Methyl α-hydrogen *cis-* and *trans-γ-o*-methoxyphenyl-γ-phenylitaconate are converted by acetic anhydride and sodium acetate into methyl 4-acetoxy-8-methoxy-1-phenyl- and methyl 4-acetoxy-1-*o*-methoxyphenyl-2-naphthoate, respectively. The ethyl esters of the *cis-* and *trans-p*-methoxy-isomers give, when similarly treated, ethyl 4-acetoxy-6-methoxy-1-phenyl- and ethyl 4-acetoxy-1-*p*-methoxyphenyl-2-naphthoate, respectively. The acetoxy-compounds are hydrolysed, then methylated and cyclised to the corresponding dimethoxy-3 : 4-benzofluorenones.

*cis-* and *trans-γ-p-* and *cis-γ-o*-Methoxyphenyl-γ-phenylitaconic anhydride yield with aluminium chloride the corresponding 1-oxo-2-indenylacetic acids, which are cyclised, then methylated to the corresponding dimethoxy-3 : 4-benzofluorenones, identical with the above compounds. However, the *trans-γ-o*-methoxyphenyl-isomer, when similarly treated, gives 4-phenyl-3-coumarinylacetic acid.

The present investigation, a continuation of a previous study (Part II),[1] deals with the Stobbe condensation of monosubstituted benzophenones with succinic esters which gives two stereoisomeric γγ-diarylitaconic acids.




**Unless otherwise stated, R¹ to R⁴ are H.**

Condensation of 2-methoxybenzophenone with dimethyl succinate gave a mixture of the expected stereoisomeric β-methyl α-hydrogen *cis-* (I; $R^2 = R^5 = OMe$, $R^6 = OH$) † and *trans-γ-o*-methoxyphenyl-γ-phenylitaconate (I; $R^3 = R^5 = OMe$, $R^6 = OH$), from which the latter was obtained crystalline and on hydrolysis gave the *trans*-acid. The mixed esters were cyclised by sodium acetate in acetic anhydride to a mixture from which both esters (II; $R^2 = R^5 = OMe$, $R^6 = OAc$) and (II; $R^3 = R^5 = OMe$, $R^6 = OAc$) were isolated. The derived phenolic acids were converted by methyl sulphate and potassium carbonate in acetone into the dimethoxy-esters (II; $R^2 = R^5 = R^6 = OMe$) and (II; $R^3 = R^5 = R^6 = OMe$), respectively. These were hydrolysed to the acids ($R^5 = OH$) which were decarboxylated to the 1-phenylnaphthalenes (III; $R^2$ or $R^3 = OMe$, $R^6 = OMe$). The product (III; $R^3 = R^6 = OMe$) was found to be identical with a specimen prepared as follows: α-Methoxynaphthalene was nitrated in acetic acid to 1-methoxy-4-nitronaphthalene [2] which was reduced by aluminium amalgam in ether to 1-methoxy-4-naphthylamine. The amine hydrochloride was converted as usual into

* Part III, *J.*, 1956, 395.

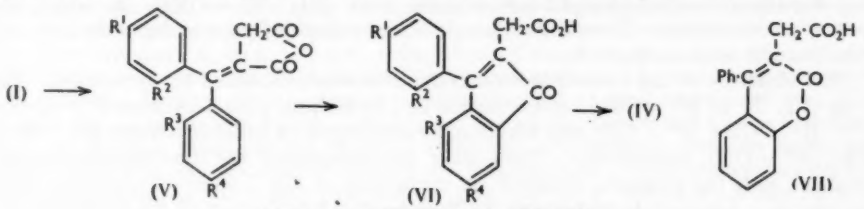
† Here and throughout this paper, all R's are H unless otherwise specified.

[1] Baddar, El-Assal, and Baghos, *J.*, 1955, 1714.

[2] Hodgson and Smith, *J.*, 1935, 671.

1-iodo-4-methoxynaphthalene,[3] identical with that obtained by the direct iodination of α-methoxynaphthalene with iodine and mercuric oxide in carbon tetrachloride.[4] Ullmann condensation of this iodo-compound with methyl 3-iodo-4-methoxybenzoate gave methyl 4 : 2′-dimethoxy-1-phenylnaphthalene-5′-carboxylate, which on hydrolysis and decarboxylation gave 4-methoxy-1-*o*-methoxyphenylnaphthalene (III; $R^3 = R^6 = OMe$). The acid (II; $R^5 = OH$, $R^2 = R^6 = OMe$) gave, on cyclisation with phosphoric oxide, 2 : 4′-dimethoxy-3 : 4-benzofluorenone (IV; $R^2 = R^6 = OMe$), whereas the acid (II; $R^5 = OH$, $R^3 = R^6 = OMe$) was best cyclised with phosphorus oxychloride [5] in *s*-tetrachloroethane, giving 2 : 5-dimethoxy-3 : 4-benzofluorenone (IV; $R^3 = R^6 = OMe$). However, cyclisation of the latter acid with phosphoric oxide afforded a mixture of the coloured fluorenone and colourless 4-methoxy-1-*o*-methoxyphenyl-2-naphthoic anhydride (predominant).

The crude mixture of acid (I; $R^2$ or $R^3 = R^5 = OMe$, $R^6 = OH$) was hydrolysed with 10% aqueous-alcoholic potassium hydroxide and *cis*- (I; $R^2 = OMe$, $R^5 = R^6 = OH$) and *trans*-γ-*o*-methoxyphenyl-γ-phenylitaconic acid (I; $R^3 = OMe$, $R^5 = R^6 = OH$) were separated by fractional crystallisation. The configuration of these acids was inferred as follows: (i) The *cis*-anhydride (V; $R^2 = OMe$) was converted by aluminium chloride in




Unless otherwise stated, $R^1$ to $R^4$ are H.

nitrobenzene into the yellow 3-*o*-methoxyphenyl-1-oxo-2-indenylacetic acid (VI; $R^2 = OMe$) which was cyclised to 2-acetoxy-4′-methoxy-3 : 4-benzofluorenone (IV; $R^2 = OMe$, $R^6 = OAc$). This was hydrolysed, then methylated, to give the dimethoxy-compound (IV; $R^2 = R^6 = OMe$). (ii) When the *trans*-anhydride (V; $R^3 = OMe$) was similarly treated, it gave the colourless 4-phenyl-3-coumarinylacetic acid (VII).

The structure of the coumarin derivative (VII) was deduced from the following facts: It was unsaturated, contained no methoxyl group, failed to give a 2 : 4-dinitrophenylhydrazone, and when refluxed with aqueous alkali and then treated with methyl sulphate [1] gave *trans*-γ-*o*-methoxyphenyl-γ-phenylitaconic acid (I; $R^3 = OMe$, $R^5 = R^6 = OH$). Its formation is attributed to the demethylating action of aluminium chloride (see Part II [1]). It was also obtained when aluminium chloride was replaced by stannic chloride, and when the *trans*-acid was treated with concentrated sulphuric acid in acetic acid.[6] The same acid was also obtained when α-methyl β-hydrogen *trans*-γ-*o*-methoxyphenyl-γ-phenylitaconate (I; $R^5 = OH$, $R^3 = R^6 = OMe$) (prepared by heating the anhydride with methanol) was heated with zinc chloride in acetic anhydride–acetic acid.[7]

When 4-methoxybenzophenone was similarly condensed with diethyl succinate, it gave an inseparable mixture of ethyl α-hydrogen *cis*- (I; $R^1 = OMe$, $R^5 = OEt$, $R^6 = OH$) and *trans*-γ-*p*-methoxyphenyl-γ-phenylitaconate (I; $R^4 = OMe$, $R^5 = OEt$, $R^6 = OEt$). The product was, therefore, cyclised directly to a mixture of ethyl naphthoates (II; $R^1$ or $R^4 = OMe$, $R^5 = OEt$, $R^6 = OAc$). Hydrolysis gave the acids ($R^5 = R^6 = OH$) which were methylated, and then decarboxylated, to give 4 : 6-dimethoxy-1-phenyl- (III; $R^1 = R^6 = OMe$) and 4-methoxy-1-*p*-methoxyphenyl-naphthalene (III; $R^4 = R^6 = OMe$).

[3] Cohen, Cook, Hewett, and Girard, *J.*, 1934, 653.
[4] Seer and Ehrenreich, *Monatsh.*, 1913, **34**, 631.
[5] (*a*) Lockett and Short, *J.*, 1939, 787; (*b*) Baddar and El-Assal, *J.*, 1951, 1844.
[6] Borsche, Gillies, Kühn, and Manteuffel, *Annalen*, 1936, **526**, 1.
[7] Johnson and Goldman, *J. Amer. Chem. Soc.*, 1945, **67**, 430.

XUM

The last compound was identical with a specimen prepared by Ullmann condensation of 1-iodo-4-methoxynaphthalene with methyl 5-bromo-2-methoxybenzoate and decarboxylation of the resulting acid.

Borsche *et al.*,[6] by cyclisation of the crude mixture of β-ethyl α-hydrogen *cis*- and *trans*-γ-*p*-methoxyphenyl-γ-phenylitaconate with sodium acetate in acetic anhydride, obtained an acetoxy-compound, which was directly hydrolysed to a phenol, m. p. 190—192°. This was claimed by them as a single compound, 4-hydroxy-*x*-methoxy-1-phenyl-2-naphthoic acid. However, it was shown in the present investigation to be a mixture of 4-hydroxy-1-*p*-methoxyphenyl- (II; $R^4 = OMe$, $R^5 = R^6 = OH$) and 4-hydroxy-6-methoxy-1-phenyl-2-naphthoic acid (II; $R^1 = OMe$, $R^5 = R^6 = OH$), m. p. 218·5—219·5° and 214—215°, respectively. The 1-phenylnaphthalene structure of the acids was supported by cyclisation to the red dimethoxy-3 : 4-benzofluorenones.

Hydrolysis of the crude mixture of ethyl hydrogen itaconates gave a mixture of acids from which one of the isomers of γ-*p*-methoxyphenyl-γ-phenylitaconic acid was isolated, but its amount was insufficient for elucidation of its stereochemical nature. The mixed acids were transformed into the anhydrides, which were treated with aluminium chloride in nitrobenzene, to give a mixture of 3-*p*-methoxyphenyl-1-oxo- (VI; $R^1 = OMe$) and 6-methoxy-1-oxo-3-phenyl-2-indenylacetic acid (VI; $R^4 = OMe$), in which the former predominated. These indenylacetic acids undoubtedly came from the *cis*- and *trans*-itaconic acids, respectively.

The structure of the 1-oxo-2-indenylacetic acids was established by cyclisation. The acids (VI; $R^1$ or $R^4 = OMe$), on cyclisation and hydrolysis, gave 4-hydroxy-2′-methoxy- (IV; $R^1 = OMe$, $R^6 = OH$) and 4-hydroxy-7-methoxy-3 : 4-benzofluorenone (IV; $R^4 = OMe$, $R^6 = OH$), respectively. These gave on methylation the dimethoxyfluorenones identical with the products obtained by cyclisation of the 1-phenyl-2-naphthoic acids (see above). Contrary to statements by Borsche *et al.*[6] cyclisation of the crude mixture of dibasic itaconic acids with concentrated sulphuric acid gave a mixture of 1-oxo-2-indenylacetic acids (VI; $R^1 = OMe$; predominant) and (VI; $R^4 = OMe$), and not the single unidentified product of m. p. 147—149°. The product of Borsche *et al.*[6] was 3-*p*-methoxyphenyl-1-oxo-2-indenylacetic acid (VI; $R^1 = OMe$).

Stobbe condensation of 2-methylbenzophenone with diethyl succinate gave a mixture of semi-solid half esters (10% yield) from which one isomer was obtained crystalline. However, 4 : 4′-dimethylbenzophenone gave β-methyl α-hydrogen γγ-di-*p*-tolylitaconate in 90% yield.

That 4 : 4′-dimethoxybenzophenone gives a higher yield (100%) than 4 : 4′-dimethylbenzophenone (90%) may be due to slight deactivation of the carbonyl group by the effect of the methyl group.

The decrease in the yield in the Stobbe condensation in the order, 4 : 4′-dimethoxy- > 2-methoxy- > 2 : 2′-dimethoxy-benzophenone, is undoubtedly due to steric factors. However, the complete failure with 2 : 2′-dimethylbenzophenone cannot be attributed to steric factors only, since even 2-methylbenzophenone gave a very much poorer yield than 2-methoxybenzophenone and 2 : 2′-dimethoxybenzophenone.[1] Although the methyl group is more bulky than the methoxyl group,[8] the difference in bulk [9] could not be solely responsible for this deactivation. Hydrogen-bond formation between the *ortho*-methyl and the carbonyl group may also be a contributing factor.

## Experimental

Light petroleum had b. p. 40—60° unless otherwise stated.

*1-Methoxy-4-nitronaphthalene.*—A mixture of nitric acid (*d* 1·42) (2·2 ml.; 1·5 mol.) and 98% acetic acid (10 ml.) was added dropwise to a stirred solution of 1-methoxynaphthalene (5·3 g.) in acetic acid (35 ml.) during 3 hr. at >10°. The mixture was kept overnight at room

[8] Williamson and Rodebush, *J. Amer. Chem. Soc.*, 1941, **63**, 3018.
[9] Braude and Forbes, *J.*, 1955, 3776.

temperature. The precipitate was filtered off (*ca.* 2·5 g.; m. p. 82—83°), and gave yellow 1-methoxy-4-nitronaphthalene (from ethanol), m. p. 84—85°. Another crop (*ca.* 1·8 g.) was obtained by the dilution of the acetic acid mother-liquor. Hodgson and Smith [2] give m. p. 85°.

1-*Methoxy*-4-*naphthylamine Hydrochloride*.—Moist aluminium amalgam (2·5 g.) was added to the ethereal solution of 1-methoxy-4-nitronaphthalene (5 g.). Working up as usual gave the amine hydrochloride (*ca.* 4·6 g.).

1-*Iodo*-4-*methoxynaphthalene*.—(i) The amine hydrochloride (3·1 g.) was converted into 1-iodo-4-methoxynaphthalene as described by Cohen *et al.*[3] The *product* was distilled (b. p. 180—200°/2 mm.) and the distillate (0·61 g.) was crystallised from light petroleum (b. p. <40°); it had m. p. 54—55° (Found: I, 43·7. $C_{11}H_9OI$ requires I, 44·7%). It was unstable at room temperature and was best stored under light petroleum in a dark, cool place.

(ii) 1-Methoxynaphthalene (3·2 g.; 1·0 mol.) was iodinated with iodine (5 g.; 1·0 atom-equiv.) in presence of mercuric oxide (2·2 g.), acetic anhydride (2 ml.), and carbon tetrachloride (30 ml.), then worked up as usual.[4] The oily product was distilled and the fraction boiling at 180—200°/2 mm. was collected and crystallised from light petroleum.

4-*Methoxy*-1-o-*methoxyphenylnaphthalene*-5′-*carboxylic Acid*.—A mixture of 1-iodo-4-methoxynaphthalene (5·6 g.), methyl 3-iodo-4-methoxybenzoate (5·8 g.), and copper bronze (7·5 g.) was heated for 5 hr. at 265—270° (ethyl cinnamate bath) with vigorous stirring, and then worked up as usual.[1] The oily product was hydrolysed with 8% methanolic sodium hydroxide (100 ml.); filtration gave the neutral product which crystallised from benzene to give 4 : 4′-dimethoxydinaphthyl, m. p. 260—261° (*ca.* 1·2 g.) (Fernholz and Piazolo [10] give m. p. 257—259°) (Found: C, 84·4; H, 5·9; OMe, 17·85. Calc. for $C_{22}H_{18}O_2$: C, 84·1; H, 5·7; OMe, 19·7%). Acidification of the alkaline solution gave acids (*ca.* 6 g.) which were methylated with dimethyl sulphate (10 g.), potassium carbonate (10·5 g.), and acetone (50 ml.). The product was extracted with boiling methanol, and the soluble fraction (4·5 g.) was hydrolysed with 8% alcoholic alkali (50 ml.) (2 hours' refluxing). The resulting acid was boiled with glacial acetic acid, and the insoluble product was identified as 2 : 2′-dimethoxydiphenyl-5 : 5′-dicarboxylic acid, m. p. >350°. Its methyl ester had m. p. 169—170°, undepressed on admixture with a specimen kindly provided by A. M. Fleifel, Faculty of Science, Cairo University. The acetic acid mother-liquor precipitated, on concentration, a colourless solid which was repeatedly crystallised from methanol, to give 4-*methoxy*-1-o-*methoxyphenylnaphthalene*-5′-*carboxylic acid*, m. p. 276—277° (*ca.* 0·5 g.) (Found: C, 74·2; H, 5·3; OMe, 19·75. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2; OMe, 20·1%).

4-*Methoxy*-1-p-*methoxyphenylnaphthalene*-3′-*carboxylic Acid*.—Condensation of 1-iodo-4-methoxynaphthalene (5·6 g.) with methyl 5-bromo-2-methoxybenzoate (5 g.) in presence of copper bronze (7·5 g.) was carried out as reported by Baddar *et al.*[11] for 5-methoxy-3-(6-methoxy-1-naphthyl)benzoic acid. The acid insoluble in benzene was identified as 4 : 4′-dimethoxydiphenyl-3 : 3-dicarboxylic acid, m. p. 236—238°, undepressed on admixture with a sample kindly provided by A. M. Fleifel. The acid soluble in benzene (2·9 g.) was esterified with diazomethane and the ester was fractionated. The fraction of b. p. 250—260°/4 mm. (*ca.* 1 g.) was hydrolysed with 8% methanolic sodium hydroxide. The acid, after being heated in a vacuum for 2 hr. at 100°, was repeatedly crystallised from methanol, to give 4-*methoxy*-1-p-*methoxyphenylnaphthalene*-3′-*carboxylic acid* (0·5 g.), m. p. 173—174° (Found: C, 73·9; H, 5·4; OMe, 21·0%).

β-*Methyl* α-*Hydrogen* γ-o-*Methoxyphenyl*-γ-*phenylitaconate*.—A solution of potassium *tert.*-butoxide [from potassium (2·2 g.) and *tert.*-butyl alcohol (50 ml.)] was treated during 20 min. with a mixture of dimethyl succinate (11 g.) and 2-methoxybenzophenone [12] (5·7 g.) in *tert.*-butyl alcohol (10 ml.). The mixture was heated for further 55 min., then worked up as usual.[1, 13] The product (6·8 g.), which solidified, crystallised from benzene–light petroleum to give β-*methyl* α-*hydrogen* trans-γ-o-*methoxyphenyl*-γ-*phenylitaconate* (I; $R^3 = R^4 = OMe$), m. p. 119—120° (1·2 g.) (Found: C, 70·4; H, 5·7; OMe, 18·0. $C_{19}H_{18}O_5$ requires C, 69·9; H, 5·5; OMe, 19·0%). The mother-liquor contained an uncrystallisable product which was probably a mixture of the *cis*- and the *trans*-ester.

*Cyclisation of* β-*Methyl* α-*Hydrogen* γ-o-*Methoxyphenyl*-γ-*phenylitaconates*.—The crude

[10] Fernholz and Piazolo, *Chem. Ber.*, 1954, **87**, 578.
[11] Baddar, Fahim, and Galaby, *J.*, 1955, 465.
[12] Ullmann and Goldberg, *Ber.*, 1902, **35**, 2811.
[13] Johnson and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 511.

XUM

mixed esters (6·5 g.), sodium acetate (1·8 g.), and acetic anhydride (30 ml.) were cyclised as described by Baddar *et al.*[1] Distillation of the solvent left a brown oil which was fractionally separated by repeated extraction with light petroleum (b. p. <40°). The soluble fraction (A) (1 g.) proved to be a mixture of methyl 4-acetoxy-1-*o*-methoxyphenyl- and 4-acetoxy-8-methoxy-1-phenyl-2-naphthoate; the insoluble fraction (B) (5 g.) was mainly the former.

*4-Hydroxy-1-o-methoxyphenyl-2-naphthoic Acid.*—Crude methyl 4-acetoxy-1-*o*-methoxyphenyl-2-naphthoate (3·7 g.) (fraction B) was hydrolysed with 10% alcoholic potassium hydroxide (10 ml.) as usual. The semi-solid acid was digested with boiling benzene, and the insoluble product crystallised from acetic acid, to give *4-hydroxy-1-o-methoxyphenyl-2-naphthoic acid*, m. p. 243—244° (Found: C, 73·0; H, 4·65; OMe, 10·65. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·8; OMe, 10·6%). The benzene mother-liquor gave an impure acid.

*Methyl 4-Methoxy-1-o-methoxyphenyl-2-naphthoate* (II; $R^3 = R^5 = R^6$ = OMe).—The acid (3 g.) was treated with dimethyl sulphate (5 g.), potassium carbonate (5·2 g.), and acetone (20 ml.) as usual. Crystallisation of the product from benzene–light petroleum gave *methyl 4-methoxy-1-o-methoxyphenyl-2-naphthoate*, m. p. 119·5—120·5° (Found: C, 74·5; H, 5·7; OMe, 26·45. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6; OMe, 28·8%). Hydrolysis of this (3·2 g.) with 10% alcoholic potassium hydroxide (10 ml.) gave the *acid*, m. p. 233—234° (from glacial acetic acid) (Found: C, 73·55; H, 5·4; OMe, 19·6. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2; OMe, 20·1%).

*4-Methoxy-1-o-methoxyphenylnaphthalene* (III; $R^3 = R^6$ = OMe).—(i) 4-Methoxy-1-*o*-methoxyphenylnaphthalene-3′-carboxylic acid (0·4 g.) was heated with copper bronze (0·5 g.) in quinoline (4 ml.) as usual.[5b] The semi-solid neutral product gave *4-methoxy-1-o-methoxyphenylnaphthalene* (0·34 g.), m. p. 89—90° [from light petroleum (b. p. 80—100°)] (Found: C, 82·5; H, 6·4; OMe, 22·9. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1; OMe, 23·5%). (ii) 4-Methoxy-1-*o*-methoxyphenyl-2-naphthoic acid (0·4 g.) was decarboxylated as in (i) (bath-temp. 205—210°). The product, crystallised from light petroleum (b. p. 80—100°), had m. p. 89—90° alone or mixed with the specimen prepared by method (i) (Found: C, 81·45; H, 6·1; OMe, 23·7%).

*2 : 5-Dimethoxy-3 : 4-benzofluorenone* (IV; $R^3 = R^6$ = OMe).—Phosphorus oxychloride (0·25 ml.) was added dropwise to a solution of 4-methoxy-1-*o*-methoxyphenyl-2-naphthoic acid (0·4 g.) in *s*-tetrachloroethane (20 ml.), then the mixture was heated for 3 hr. at 140—150°, and worked up as usual.[5] The red product (0·3 g.), crystallised from benzene–light petroleum, gave *2 : 5-dimethoxy-3 : 4-benzofluorenone* in red needles, m. p. 167—168° (Found: C, 78·25; H, 4·8; OMe, 19·75. $C_{19}H_{14}O_3$ requires C, 78·6; H, 4·8; OMe, 21·4%). When the cyclisation was carried out with phosphoric oxide in benzene, a mixture of the above fluorenone and a colourless product (predominant) was obtained. The latter, crystallised from benzene, gave *4-methoxy-1-o-methoxyphenyl-2-naphthoic anhydride*, m. p. 220—221° (Found: C, 76·7; H, 5·1. OMe, 19·3. $C_{38}H_{30}O_7$ requires C, 76·25; H, 5·0; OMe, 20·7%). Its structure was established by hydrolysis with 20% sodium hydroxide solution to 4-methoxy-1-*o*-methoxy-1-naphthoic acid.

*Methyl 4 : 8-Dimethoxy-1-phenyl-2-naphthoate* (II; $R^3 = R^5 = R^6$ = OMe).—Crude methyl 4-acetoxy-8-methoxy-1-phenyl-2-naphthoate (1 g.) (fraction A) was hydrolysed by 10% alcoholic potassium hydroxide. Crystallisation of the product from benzene gave 4-hydroxy-1-*o*-methoxyphenyl-2-naphthoic acid, m. p. and mixed m. p. 243—244° (*ca.* 0·2 g.). Distillation of the benzene mother-liquor left a semi-solid mass (*ca.* 0·7 g.) which was methylated with dimethyl sulphate (1·2 g.), potassium carbonate (1·4 g.), and acetone (15 ml.). The product was distilled and the fraction boiling at 250—260°/2 mm. was repeatedly crystallised from methanol, to give *methyl 4 : 8-dimethoxy-1-phenyl-2-naphthoate* (*ca.* 0·3 g.), m. p. 127—128° (depressed to 95—115° on admixture with a specimen of its isomer) (Found: C, 74·5; H, 5·6; OMe, 26·2. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6; OMe, 28·8%).

Hydrolysis of this ester (0·3 g.) with 10% alcoholic potassium hydroxide (10 ml.) (2 hours' refluxing) gave *4 : 8-dimethoxy-1-phenyl-2-naphthoic acid* in colourless aggregates (from benzene–light petroleum), m. p. 180—181°, depressed to 110—120° on admixture with its isomer (Found: C, 74·3; H, 5·15; OMe, 20·7%).

*cis- and* trans-*γ-o-Methoxyphenyl-γ-phenylitaconic Acid.*—The crude mixture of β-methyl α-hydrogen *cis-* and *trans-γ-o*-methoxyphenyl-*γ*-phenylitaconate (6·8 g.) was hydrolysed with 10% alcoholic potassium hydroxide (50 ml.). The semi-solid acid (*ca.* 6 g.) was triturated with ether, then repeatedly crystallised from acetic acid, to give *trans-γ-o-methoxyphenyl-γ-phenylitaconic acid*, m. p. 201—202° (*ca.* 2·5 g.) (Found: C, 68·7; H, 5·1; OMe, 10·35. $C_{18}H_{16}O_5$

requires C, 69·2; H, 5·1; OMe, 9·9%). The ether used for trituration was evaporated and the residue repeatedly crystallised from benzene, to give cis-γ-o-*methoxyphenyl-γ-phenylitaconic acid* (1·8 g.), m. p. 154—155°, depressed to 105—115° on admixture with the isomer (Found: C, 69·7; H, 5·2; OMe, 9·8%). Hydrolysis of the pure *trans*-half ester (I; $R^3 = R^5 = OMe$, $R^6 = OH$), m. p. 119—120°, gave an acid of m. p. 201—202°, undepressed on admixture with the *trans*-acid.

trans-γ-o-*Methoxyphenyl-γ-phenylitaconic Anhydride* (V; $R^3 = OMe$).—The *trans*-acid, m. p. 201—202° (3 g.), was refluxed with acetyl chloride (30 ml.) for an hour, and then worked up as usual. The product (*ca.* 3 g.) crystallised from benzene–light petroleum, to give trans-γ-o-*methoxyphenyl-γ-phenylitaconic anhydride*, m. p. 155—156° (Found: C, 73·6; H, 4·7; OMe, 10·7. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·8; OMe, 10·6%).

cis-γ-o-*Methoxyphenyl-γ-phenylitaconic Anhydride* (V; $R^3 = OMe$).—The *cis*-acid, m. p. 154—155° (2 g.), was similarly treated (2 hours' refluxing), giving cis-γ-o-*methoxyphenyl-γ-phenylitaconic anhydride* (*ca.* 1·8 g.), m. p. 157—158°, depressed to 128—136° on admixture with its isomer and to 133—140° on admixture with its acid (Found: C, 73·8; H, 5·0; OMe, 10·45%).

α-*Methyl* β-*Hydrogen* trans-γ-o-*Methoxyphenyl-γ-phenylitaconate.*—*trans*-γ-o-Methoxyphenyl-γ-phenylitaconic anhydride (1 g.) and absolute methanol (20 ml.) were refluxed for 3 hr., then worked up as usual.[13] Crystallisation from benzene–light petroleum gave α-*methyl* β-*hydrogen* trans-γ-o-*methoxyphenyl-γ-phenylitaconate*, m. p. 140—141°, depressed to 105—115° on admixture with a specimen of the *trans*-half ester obtained by Stobbe condensation (Found: C, 69·9; H, 5·6; OMe, 18·5. $C_{19}H_{18}O_5$ requires C, 69·9; H, 5·5; OMe, 19·0%).

When the above anhydride was similarly treated with absolute ethanol, the corresponding *ethyl ester*, m. p. 132—133° (from benzene–light petroleum), was obtained (Found: C, 70·6; H, 6·0. $C_{20}H_{20}O_5$ requires C, 70·6; H, 5·9%).

4-*Phenyl-3-coumarinylacetic Acid* (VII).—(i) The *trans*-anhydride (3 g.) was treated in nitrobenzene (30 ml.) with aluminium chloride (2 g.), and worked up as described by Baddar *et al.*[1] Crystallisation of the product from benzene gave 4-*phenyl-3-coumarinylacetic acid*, m. p. 189—190°, depressed to 170—175° on admixture with *trans*-γ-o-methoxyphenyl-γ-phenylitaconic acid (Found: C, 72·75; H, 4·3; OMe, 0. $C_{17}H_{12}O_4$ requires C, 72·85; H, 4·3%). (ii) The same anhydride (0·4 g.) and stannic chloride (4 ml.) in *s*-tetrachloroethane (15 ml.) were refluxed at 130—140° for 3 hr. The product, crystallised from benzene, gave the coumarinylacetic acid (0·35 g.), m. p. 189—190°. (iii) The *trans*-half ester (I; $R^3 = OMe$, $R^5 = OH$, $R^6 = OEt$) (0·6 g.), m. p. 132—133°, acetic anhydride (7·5 ml.), glacial acetic acid (7·5 ml.), and zinc chloride (0·08 g.) were refluxed for 2 hr.,[7] then worked up as usual. The oily product (0·6 g.) was hydrolysed with 3% alcoholic potassium hydroxide (10 ml.) (2 hr.). Acidification of the alkaline solution precipitated an acid which on crystallisation from benzene gave the same coumarinylacetic acid, m. p. and mixed m. p. 189—190°. (iv) The *trans*-itaconic acid (I; $R^3 = OMe$; $R^5 = R^6 = OH$) (0·4 g.) was cyclised with concentrated sulphuric acid (40 ml.) and acetic acid (2 ml.), then worked up as described by Borsche *et al.*[6] The product, crystallised from benzene, gave the same coumarinylacetic acid, m. p. and mixed m. p. 189—190°.

*Conversion of* 4-*Phenyl-3-coumarinylacetic Acid into* trans-γ-o-*Methoxyphenyl-γ-phenylitaconic Acid* (I; $R^3 = OMe$, $R^5 = R^6 = OH$).—A solution of the coumarinylacetic acid (0·5 g.) in sodium hydroxide (0·4 g.) and water (4·5 ml.) was refluxed for 30 min., then heated on the water-bath with dimethyl sulphate (0·8 g.) for 5 hr.[1,14] Crystallisation of the product from acetic acid gave the *trans*-itaconic acid, m. p. and mixed m. p. 201—202° (0·5 g.).

3-o-*Methoxyphenyl*-1-*oxo*-2-*indenylacetic Acid* (VI; $R^3 = OMe$).—Finely powdered aluminium chloride (1·4 g.) was added gradually to a solution of *cis*-γ-o-methoxyphenyl-γ-phenylitaconic anhydride (2 g.) in nitrobenzene (20 ml.), and worked up as usual.[1] The yellow product, crystallised from benzene, gave the yellow *indenylacetic acid*, m. p. 189—190°, depressed to 150—165° on admixture with the coumarinylacetic acid (Found: C, 73·6; H, 4·8; OMe, 11·8. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·8; OMe, 10·5%). Its 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid in orange-red needles, m. p. 264—265° (Found: N, 11·2. $C_{24}H_{18}O_7N_4$ requires N, 11·8%).

2-*Acetoxy*-4′-*methoxy*-3 : 4-*benzofluorenone* (IV; $R^3 = OMe$, $R^6 = OAc$).—The above indenylacetic acid (2 g.) and sodium acetate (0·8 g.) in acetic anhydride (20 ml.) were refluxed for 5 hr.,

[14] Stoermer and Friemel, *Ber.*, 1911, **44**, 1838.

then worked up. Crystallisation of the product from acetic acid gave *2-acetoxy-4'-methoxy-3 : 4-benzofluorenone* in red needles, m. p. 180—181° (Found: C, 75·4; H, 4·2; OMe, 8·65. $C_{20}H_{14}O_4$ requires C, 75·5; H, 4·4; OMe, 9·75%).

*2-Hydroxy-4'-methoxy-3 : 4-benzofluorenone* (IV; $R^2$ = OMe, $R^6$ = OH).—The acetoxybenzofluorenone (2 g.) with boiling N-sodium hydroxide (10 ml.) gave in 2 hr. the *hydroxybenzofluorenone*, dark-red needles, m. p. 261—263° (from acetic acid) (Found: C, 77·8; H, 4·25; OMe, 12·2. $C_{18}H_{12}O_3$ requires C, 78·3; H, 4·35; OMe, 11·2%).

*2 : 4'-Dimethoxy-3 : 4-benzofluorenone* (IV; $R^2 = R^6$ = OMe).—(i) A mixture of 4 : 8-dimethoxy-1-phenyl-2-naphthoic acid (0·6 g.), benzene (15 ml.), and phosphoric oxide (0·3 g.) was refluxed for 2 hr. The product, crystallised from benzene–light petroleum, gave *2 : 4'-dimethoxy-3 : 4-benzofluorenone*, red needles, m. p. 148—149° (Found: C, 78·45; H, 4·9; OMe, 20·95. $C_{19}H_{14}O_3$ requires C, 78·6; H, 4·8; OMe, 21·4%). (ii) 2-Hydroxy-4'-methoxy-3 : 4-benzofluorenone (0·5 g.), dimethyl sulphate (0·3 g.), potassium carbonate (0·3 g.), and acetone (15 ml.) gave 2 : 4-dimethoxy-3 : 4-benzofluorenone in red needles, m. p. and mixed m. p. 148—149° (from benzene–light petroleum).

*β-Ethyl α-Hydrogen* cis- *and* trans-*γ*-p-*Methoxyphenyl-γ-phenylitaconate*.—4-Methoxybenzophenone[12] (5·7 g.), diethyl succinate (6·5 g.), and a solution of potassium *tert.*-butoxide [from potassium (1·1 g.) and *tert.*-butyl alcohol (25 ml.)] was refluxed for 20 min. under nitrogen. An equal amount of potassium *tert.*-butoxide solution (25 ml.) was added and the mixture was refluxed for a further 20 min.,[1, 13] then worked up as usual. The product (*ca.* 8·2 g., 90%) was uncrystallisable. Borsche *et al.*[6] obtained a 75% yield when using sodium ethoxide.

*Ethyl 4-Acetoxy-6-methoxy-1-phenyl-* and *Ethyl 4-acetoxy-*p-*methoxyphenyl-2-naphthoate*.—The crude mixture of the above stereoisomeric half-esters (8·5 g.), sodium acetate (2 g.), and acetic anhydride (60 ml.) was refluxed for 5 hr., and worked up as usual. The oily product (*ca.* 8·0 g.) was triturated with ethanol (30 ml.), then repeatedly crystallised from the same solvent to give *ethyl 4-acetoxy-6-methoxy-1-phenyl-2-naphthoate* (II; $R^1$ = OMe, $R^5$ = OEt, $R^6$ = OAc) (3 g.), m. p. 125—126° (Found: C, 72·15; H, 5·4. $C_{22}H_{20}O_5$ requires C, 72·5; H, 5·5%). The alcohol used in trituration slowly gave another crop, m. p. 80—82° (*ca.* 1·8 g.). This on repeated crystallisation from benzene–light petroleum gave *ethyl 4-acetoxy-*1-p-*methoxy-2-naphthoate* (*ca.* 1·8 g.), m. p. 87—88°, depressed to 65—70° on admixture with a specimen of the above isomer (Found: C, 72·8; H, 5·45; OMe, 16·6%). Borsche *et al.*[6] did not obtain these acetoxy-derivatives crystalline.

*4-Hydroxy-*1-p-*methoxyphenyl-2-naphthoic Acid* (II; $R^4$ = OMe, $R^5 = R^6$ = OH).—This was obtained in a quantitative yield by hydrolysis of the corresponding acetoxy-ester with 10% alcoholic potassium hydroxide. Crystallisation from acetic acid gave the *acid*, m. p. 218·5—219·5°, depressed to 190—195° on admixture with its isomer (II; $R^1$ = OMe, $R^5 = R^6$ = OH) (Found: C, 73·4; H, 4·7; OMe, 11·75. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·8; OMe, 10·6%).

When the crude acetoxy-esters, m. p. 120—122°, were hydrolysed, and the acid was crystallised from methylene chloride, a crystalline product, m. p. 190—192°, was obtained (cf. Borsche *et al.*[6]). This was an inseparable mixture of the isomeric phenolic acids. The *methyl ester* (obtained by use of methanol and hydrogen chloride and crystallised from benzene) had m. p. 160—161° (Found: C, 73·65; H, 5·2; OMe, 20·0. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2; OMe, 20·1%).

*Methyl 4-Methoxy-*1-p-*methoxyphenyl-2-naphthoate* (II; $R^4 = R^5 = R^6$ = OMe).—The hydroxy-acid (3 g.) was methylated with dimethyl sulphate (5 g.), potassium carbonate (5·2 g.), and acetone (20 ml.). The product, crystallised from benzene–light petroleum, gave *methyl 4-methoxy-*1-p-*methoxyphenyl-2-naphthoate*, m. p. 121—122° (Found: C, 73·95; H, 5·7; OMe, 27·25. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6; OMe, 28·8%). Hydrolysis of the ester with 15% alcoholic potassium hydroxide gave *4-methoxy-*1-p-*methoxyphenyl-2-naphthoic acid*, m. p. 204—205° (from acetic acid), depressed to 178—200° on admixture with its isomer (Found: C, 74·0; H, 5·1; OMe, 19·6%).

*4-Methoxy-*1-p-*methoxyphenylnaphthalene* (III; $R^4 = R^6$ = OMe).—(i) *Decarboxylation of 4-methoxy-*1-p-*methoxyphenylnaphthalene-3'-carboxylic acid*. The acid (0·4 g.) was heated with copper bronze (0·5 g.) in quinoline (4 ml.), and worked up as usual. Crystallisation of the oily product from benzene–light petroleum (b. p. 80—100°) gave *4-methoxy-*1-p-*methoxyphenylnaphthalene* (0·34 g.), m. p. 104—105° (Found: C, 81·9; H, 6·1; OMe, 20·6. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1; OMe, 23·5%).

(ii) *Decarboxylation* of *4-methoxy-*1-p-*methoxyphenyl-2-naphthoic acid*. The acid (0·4 g.)

was decarboxylated as in (i), and the product crystallised from the same solvent to give 4-methoxy-1-*p*-methoxyphenylnaphthalene (0·35 g.), m. p. and mixed m. p. 104—105°. Its m. p. was depressed to 70—80° on admixture with a specimen of 4 : 6-dimethoxy-1-phenylnaphthalene (see below) (Found: C, 81·8; H, 6·1; OMe, 20·2%).

*4-Hydroxy-6-methoxy-1-phenyl-2-naphthoic Acid* (II; $R^1$ = OMe, $R^3$ = $R^6$ = OH).—This was obtained by the hydrolysis of the acetoxy-ester (3·7 g.) with 10% alcoholic potassium hydroxide. Crystallisation of the product from dilute acetic acid gave *4-hydroxy-6-methoxy-1-phenyl-2-naphthoic acid* (*ca.* 3 g.), m. p. 214—215° (Found: C, 72·9; H, 4·9; OMe, 9·9. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·8; OMe, 10·6%). Its *methyl ester* (methanol and hydrogen chloride), crystallised from benzene, had m. p. 216—217° (Found: C, 74·1; H, 5·2; OMe, 19·9. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2; OMe, 20·1%).

*Methyl 4 : 6-Dimethoxy-1-phenyl-2-naphthoate.*—The phenolic acid (3 g.), methylated with dimethyl sulphate (5 g.), potassium carbonate (5·2 g.), and acetone (20 ml.), gave *methyl 4 : 6-dimethoxy-1-phenyl-2-naphthoate* (3·2 g.), m. p. 135·5—136·5° (from benzene–light petroleum) (Found: C, 74·8; H, 5·7; OMe, 27·05. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6; OMe, 28·8%). Hydrolysis of the ester with 10% alcoholic potassium hydroxide gave the *4 : 6-dimethoxy-acid*, m. p. 233—234° (from acetic acid) (*ca.* 3 g.) (Found: C, 73·7; H, 5·15; OMe, 21·1. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2; OMe, 20·1%).

*4 : 6-Dimethoxy-1-phenylnaphthalene.*—The preceding acid (0·4 g.) was decarboxylated with copper bronze (0·5 g.) in quinoline (4 ml.) at 205—210°; crystallisation from light petroleum (b. p. 80—100°) gave *4 : 6-dimethoxy-1-phenylnaphthalene* (0·35 g.), m. p. 101—102°, depressed to 70—80° on admixture with a specimen of the isomeric 4-methoxy-1-*p*-methoxyphenylnaphthalene (Found: C, 82·2; H, 5·9; OMe, 25·6. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1; OMe, 23·5%).

*γ-p-Methoxyphenyl-γ-phenylitaconic Acid.*—The mixed half-esters (I; $R^1$ or $R^4$ = OMe, $R^3$ = OEt, $R^6$ = OH) (8·5 g.) was hydrolysed with 10% alcoholic potassium hydroxide (50 ml.). Fractional crystallisation from ether gave a *γ-p-methoxyphenyl-γ-phenylitaconic acid* (*ca.* 0·8 g.), m. p. 183—184° (Borsche *et al.*[6] did not obtain a crystalline product) (Found: C, 69·3; H, 5·1; OMe, 9·25. $C_{18}H_{16}O_5$ requires C, 69·2; H, 5·1; OMe, 9·9%). Evaporation of the ethereal mother-liquor gave an inseparable mixture of acids, m. p. 145—149° (cleared with gas evolution).

The mixed acids (7·5 g.) were refluxed with acetyl chloride (50 ml.). The anhydrides (7·4 g.) failed to solidify and were used in the following step.

*3-p-Methoxyphenyl-1-oxo-* and *6-Methoxy-1-oxo-3-phenyl-2-indenylacetic Acid.*—A solution of the above anhydrides (7·4 g.) in nitrobenzene (60 ml.) was treated with aluminium chloride (4 g.) as described for the *o*-methoxy-derivative. The product was fractionally crystallised from benzene, to give *3-p-methoxyphenyl-1-oxo-2-indenylacetic acid* (*ca.* 3 g.) in orange-yellow crystals, m. p. 152—153°, identical with the unidentified product, m. p. 147—149°, obtained by Borsche *et al.*[6] (Found: C, 74·1; H, 4·5; OMe, 10·1. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·8; OMe, 10·6%). Its *2 : 4-dinitrophenylhydrazone* was obtained in orange-red needles (from acetic acid), m. p. 250—251° (Found: N, 11·8. $C_{24}H_{18}O_7N_4$ requires N, 11·8%). Borsche *et al.*[6] give m. p. ≯250°.

Concentration of the benzene mother-liquor precipitated another fraction which was repeatedly crystallised from the same solvent, to give orange-red *6-methoxy-1-oxo-3-phenyl-2-indenylacetic acid* (*ca.* 0·5 g.), m. p. 175·5—176·5°, depressed to 120—130° on admixture with the isomer (Found: C, 73·8; H, 4·8; OMe, 11·35%). Its *2 : 4-dinitrophenylhydrazone* was obtained in red crystals (from dioxan), m. p. 263—264°, depressed to 230—240° on admixture with the above hydrazone (Found: N, 12·1%). Contrary to Borsche *et al.*[6] cyclisation of the crude mixture of the itaconic acids with sulphuric acid gave mixed acids.

*2-Acetoxy-2′-methoxy-3 : 4-benzofluorenone* (IV; $R^1$ = OMe, $R^6$ = OAc).—*3-p*-Methoxyphenyl-1-oxo-2-indenylacetic acid (3 g.) was cyclised with sodium acetate (1 g.) in acetic anhydride (20 ml.) as usual. Crystallisation of the product (3·1 g.) from acetic acid gave *2-acetoxy-2′-methoxy-3 : 4-benzofluorenone* in yellow plates, m. p. 212—213° (Borsche *et al.*[6] give m. p. 209—210° for an unidentified product) (Found: C, 74·9; H, 4·2; OMe, 10·1. $C_{20}H_{14}O_4$ requires C, 75·5; H, 4·4; OMe, 9·75%). Hydrolysis of this compound (2 g.) with N-aqueous sodium hydroxide (10 ml.) (2 hr.) gave *2-hydroxy-2′-methoxy-3 : 4-benzofluorenone* in dark red needles (from acetic acid), m. p. 351—352°, depressed to 255—258° on admixture with its isomer (Found: C, 77·7; H, 4·25; OMe, 10·25. $C_{18}H_{12}O_3$ requires C, 78·3; H, 4·35; OMe, 11·2%). Borsche *et al.*[6] give m. p. 255—258° for the unidentified product obtained by

cyclisation of the impure acid, m. p. 190—192°. This was probably a mixture of the two isomeric hydroxy-3 : 4-benzofluorenones.

2 : 2′-*Dimethoxy*-3 : 4-*benzofluorenone* (IV; $R^1 = R^6 = OMe$).—(i) *Cyclisation of* 4 : 6-*dimethoxy*-1-*phenyl*-2-*naphthoic acid.* This was carried out with phosphoric oxide in benzene. Crystallisation of the product from benzene gave 2 : 2′-*dimethoxy*-3 : 4-*benzofluorenone* in red crystalline aggregates, m. p. 175—176° (Found: C, 78·25; H, 4·7; OMe, 25·3. $C_{19}H_{14}O_3$ requires C, 78·6; H, 4·8; OMe, 21·4%).

(ii) *Etherification of* 2-*hydroxy*-2′-*methoxy*-3 : 4-*benzofluorenone.* This was carried out by dimethyl sulphate, potassium carbonate, and acetone. On crystallisation from benzene, 2 : 2′-dimethoxy-3 : 4-benzofluorenone was obtained in red aggregates (0·5 g.), m. p. and mixed m. p. 175—176° (Found: C, 78·2; H, 4·7; OMe, 19·6%).

2-*Acetoxy*-7-*methoxy*-3 : 4-*benzofluorenone.*—6-Methoxy-1-oxo-3-phenyl-2-indenylacetic acid (0·6 g.) was cyclised with sodium acetate (0·4 g.) in acetic anhydride (10 ml.). On crystallisation from acetic acid, 2-*acetoxy*-7-*methoxy*-3 : 4-*benzofluorenone* (0·5 g.) was obtained in red crystals, m. p. 207—208°, depressed to 168—175° (shrinkage at 160°) on admixture with 2-acetoxy-2′-methoxy-3 : 4-benzofluorenone (Found: C, 75·45; H, 4·4; OMe, 9·65. $C_{20}H_{14}O_4$ requires C, 75·5; H, 4·4; OMe, 9·75%). This compound (0·5 g.) was hydrolysed with N-aqueous sodium hydroxide (10 ml.) to 2-hydroxy-7-methoxy-3 : 4-benzofluorenone, red crystals (from acetic acid), m. p. >350°.

2 : 7-*Dimethoxy*-3 : 4-*benzofluorenone.*—(i) *Cyclisation* of 4-*methoxy*-1-p-*methoxyphenyl*-2-*naphthoic acid.* The acid was cyclised with phosphoric oxide in benzene, and the product crystallised from benzene to give 2 : 7-*dimethoxy*-3 : 4-*benzofluorenone* in red needles (0·5 g.), m. p. 184—185°, depressed to 140—150° on admixture with 2 : 2′-dimethoxy-3 : 4-benzofluorenone (Found: C, 78·25; H, 4·9; OMe, 19·2. $C_{19}H_{14}O_3$ requires C, 78·6; H, 4·8; OMe, 21·4%).

(ii) *Methylation of* 2-*hydroxy*-7-*methoxy*-3 : 4-*benzofluorenone.* The phenol was methylated as usual. Crystallisation from benzene gave 2 : 7-dimethoxy-3 : 4-benzofluorenone (0·5 g.), m. p. and mixed m. p. 184—185° (Found: C, 78·3; H, 4·7; OMe, 19·4%).

*γγ-Di*-p-*tolylitaconic Acid.*—4 : 4′-Dimethylbenzophenone (5·3 g.) was condensed with dimethyl succinate (11 g.) in the presence of a solution of potassium *tert.*-butoxide [from potassium (2·2 g.) in *tert.*-butyl alcohol (50 ml.)] (1·5 hours' refluxing). β-Methyl α-hydrogen *γγ*-di-*p*-tolylitaconate was hydrolysed by 10% alcoholic potassium hydroxide to *γγ-di*-p-*tolylitaconic acid* (7 g., 90%), m. p. 169·5—170·5° (from dilute ethanol) (Found: C, 73·3; H, 5·8. $C_{19}H_{18}O_4$ requires C, 73·55; H, 5·8%). The *anhydride*, m. p. 118·5—119·5° (from benzene–light petroleum), was obtained by refluxing the acid (3 g.) with acetyl chloride (20 ml.) (Found: C, 77·8; H, 5·8. $C_{19}H_{16}O_3$ requires C, 78·1; H, 5·5%).

β-*Ethyl* α-*Hydrogen* cis- *and* trans-*γ*-*Phenyl*-*γ*-o-*tolylitaconate.*—2-Methylbenzophenone (4·9 g.) was condensed with dimethyl succinate (13 g.) as described for 2-methoxybenzophenone. The oily half-ester (0·9 g., 10%) was left at 25—30° for several days, triturated with benzene–light petroleum, then repeatedly crystallised from the same solvent, to give β-*ethyl* α-*hydrogen* cis- or trans-*γ*-*phenyl*-*γ*-o-*tolylitaconate* (*ca.* 0·3 g.), m. p. 115—116° (Found: C, 74·3; H, 6·25. $C_{20}H_{20}O_4$ requires C, 74·1; H, 6·2%).

CHEMISTRY DEPARTMENT, FACULTY OF SCIENCE,
CAIRO UNIVERSITY, CAIRO.

[*Received, July 19th,* 1957.]

## 199. *The Behaviour of Derivatives of* 3 : 4-*Anhydrogalactose towards Acidic Reagents. Part I.*

By J. G. Buchanan.

The product arising from alkaline hydrolysis of methyl 2 : 3-di-*O*-benzoyl-4-*O*-tosyl-6-*O*-triphenylmethyl-α-D-glucoside [1] (I) is shown to be a mixture of methyl 3 : 4-anhydro-6-*O*-triphenylmethyl-α-D-galactoside (V) and methyl 2 : 3-anhydro-6-*O*-triphenylmethyl-α-D-guloside (XXI). The structures of several compounds made during earlier investigations of this problem [1,2] have been elucidated.

The behaviour of methyl 3 : 4-anhydro-β-D-galactoside [3] towards acidic reagents was investigated by Müller.[4,5] Dilute sulphuric acid was shown to yield a mixture of D-gulose and D-glucose,[5] in agreement with the well-known steric course of these reactions.[6] Oldham and Robertson [1] prepared methyl 3 : 4-anhydro-6-*O*-triphenylmethyl-α-D-galactoside (V) by treatment of methyl 2 : 3-di-*O*-benzoyl-4-*O*-tosyl-6-*O*-triphenylmethyl-α-D-glucoside (I) with alkali. The compound was not crystalline, nor was its 2-acetate (IV). The acetate (IV), with acetone containing dry hydrogen chloride, gave a mixture from which mono-*O*-acetyl-*O*-*iso*propylidene derivatives of methyl α-D-galactoside and methyl α-D-guloside were isolated. Reaction of a sugar epoxide with acid or alkaline reagents normally yields *trans*-products.[6] The reaction of the 3 : 4-anhydrogalactoside with acetone involved both *cis*- and *trans*-opening of the epoxide ring. It is known, moreover, that aqueous hydrochloric acid in acetone causes *trans*-opening of an epoxide ring, to give chlorohydrins.[7] These apparent inconsistencies led to a re-investigation of the problem by Labaton and Newth.[2]

These authors confirmed the earlier work and made certain other observations on the structures of the *iso*propylidene compounds. The galactoside had been deacetylated by Oldham and Robertson to a methyl *O*-*iso*propylidene-α-D-galactoside which, from its properties, was clearly the 3 : 4-cyclic acetal; Labaton and Newth therefore assigned structure (VII) to the acetate. The guloside was converted into a toluene-*p*-sulphonate in which the sulphonyloxy-group was stable to treatment with sodium iodide. The original acetate had therefore structure (VIII), giving the derivative (IX). No sugars other than galactose or gulose were present in acid hydrolysates of the total deacetylated mixture.

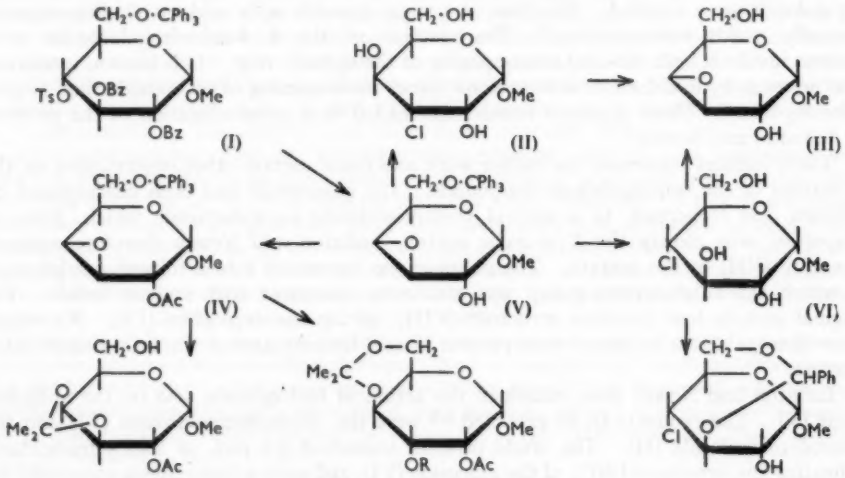
Labaton and Newth then examined the action of hydrochloric acid on the anhydrosugar (V). The products to be expected [8,9] were the chlorodeoxyglucoside (VI) and the chlorodeoxyguloside (II). The crude product consumed 0·4 mol. of lead tetra-acetate, indicating the presence of 40% of the glucoside (VI), and gave a benzylidene compound on treatment with benzaldehyde and zinc chloride. The other chlorodeoxy-sugar was isolated from the aqueous mother-liquors. It was expected that the sugar which had reacted with benzaldehyde would be the guloside (II) but it was found, after hydrolysis of the benzylidene residue, that the chlorodeoxy-sugar consumed 1 mol of periodate. It was therefore assigned the glucoside structure (VI) and the benzylidene compound the 3 : 6-structure (X). The other sugar did not react with periodate and was therefore the guloside (II). When either chlorodeoxy-sugar was treated with sodium methoxide the same halogen-free product, presumably methyl 3 : 4-anhydro-α-D-galactoside (III), was

[1] Oldham and Robertson, *J.*, 1935, 685.
[2] Labaton and Newth, *J.*, 1953, 992.
[3] Helferich and Müller, *Ber.*, 1930, **63**, 2142.
[4] Müller, *Ber.*, 1934, **67**, 421.
[5] *Idem*, *Ber.*, 1935, **68**, 1094.
[6] Peat, *Adv. Carbohydrate Chem.*, 1946, **2**, 51.
[7] Robertson and Dunlop, *J.*, 1938, 472.
[8] Newth, Overend, and Wiggins, *J.*, 1947, 10.
[9] Newth and Homer, *J.*, 1953, 989.

XUM

obtained; it did not give a triphenylmethyl derivative. Most of this analysis is summarised in Scheme I. The more recent work, while it confirmed the earlier observations, seemed to present more difficulties. While 3 : 6-*O*-benzylidene compounds in the glucose series are sterically possible, this is the only known example. The problem of both *cis*- and *trans*-opening of the epoxide ring by acetone remained.

It appeared that Lake and Peat's results [10] on derivatives of 2 : 3-anhydromannose might have some bearing.[11] When methyl 3 : 4 : 6-tri-*O*-acetyl-2-*O*-tosyl-β-D-glucoside (XI) is treated with sodium methoxide, derivatives of both the 2 : 3-anhydromannoside (XII) and the 3 : 4-anhydroaltroside (XIII) can be isolated. The 3-hydroxyl group in the mannoside, the anhydro-sugar which is formed first, is *trans* to the epoxide ring and can yield the altroside; the reaction is probably reversible. In the 3 : 4-anhydrogalactoside (V) the situation is similar and one might expect to have some of the 2 : 3-anhydroguloside (XXI) produced. Newth,[12] Overend and Ricketts,[13] and Angyal and Gilham [14] have recently cited other examples of this phenomenon. Methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-guloside [15] (XV) was therefore treated with hydrochloric acid in acetone.[7] The benzylidene group was removed during the reaction and a methyl chlorodeoxyhexoside was isolated directly from the reaction mixture in 42% yield.[11] Since the product consumed 1 mol. of periodate, it was the 2-chloro-2-deoxyidoside (XVI). It had the same




Scheme I.

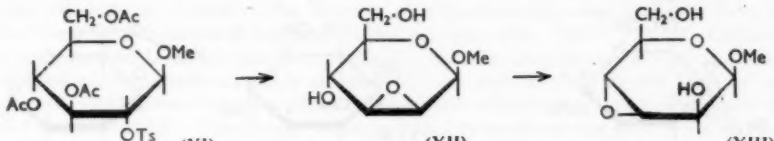
melting point as, and similar rotation to, Labaton and Newth's " chlorodeoxyglucoside; " its benzylidene compound (XIV) was identical with " methyl 3 : 6-*O*-benzylidene-4-chloro-4-deoxy-α-D-glucoside," [2] and the latter gave a quantitative yield of methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-guloside on treatment with sodium methoxide. These experiments showed clearly that the 2 : 3-anhydroguloside (XXI) was present in appreciable amounts in earlier preparations of methyl 3 : 4-anhydro-6-*O*-triphenylmethyl-α-D-galactoside. The other methyl chlorodeoxyhexoside isolated by Labaton

[10] Lake and Peat, *J.*, 1939, 1069.
[11] Buchanan, *Chem. and Ind.*, 1954, 1484.
[12] Newth, *J.*, 1956, 441.
[13] Overend and Ricketts, *Chem. and Ind.*, 1957, 632.
[14] Angyal and Gilham, *J.*, 1957, 3691.
[15] Reichstein and Sorkin, *Helv. Chim. Acta*, 1945, **28**, 1.

and Newth could then have one of three structures: the 3-chloro-3-deoxyguloside (II), the 4-chloro-4-deoxyglucoside (VI) (both derived from the 3 : 4-anhydrogalactoside), or a 3-chloro-3-deoxygalactoside derived from the 2 : 3-anhydroguloside. Of these, the guloside and galactoside are capable of forming 4 : 6-benzylidene derivatives and would be stable to periodate; the glucoside cannot form a cyclic 4 : 6-acetal, but contains an α-glycol system.

The chlorodeoxyhexoside was therefore isolated and found to reduce 1·03 mol. of periodate in 7 days; Labaton and Newth's " methyl 3-chloro-3-deoxy-α-D-guloside " was therefore the 4-chloro-4-deoxyglucoside (VI). The slow periodate consumption was in agreement with the results of periodate oxidation of certain other 4-substituted glucosides.[16,17]

The *iso*propylidene compounds resulting from the reaction with dry acetone and hydrogen chloride were then studied. The galactoside was shown to be methyl 6-*O*-acetyl-




(XI) (XII) (XIII)

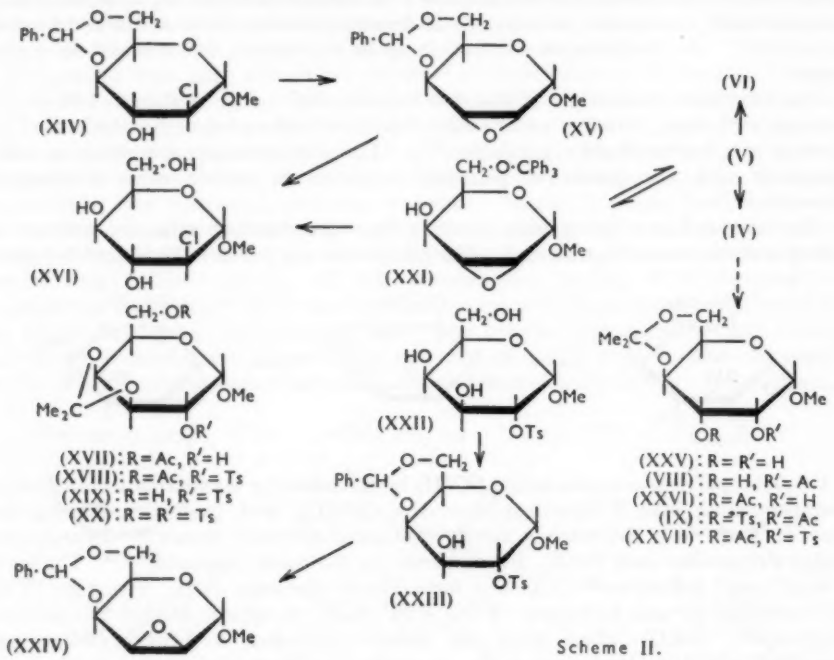
3 : 4-*O*-*iso*propylidene-α-D-galactoside (XVII) by the following transformations. Toluene-*p*-sulphonylation gave a crystalline derivative (XVIII), with properties differing from those of Iselin and Reichstein's syrupy 2-*O*-acetyl-6-*O*-tosyl isomer.[18] Deacetylation yielded a crystalline ester (XIX), different from the 6-*O*-tosyl compound.[18,19] The known 2 : 6-di-*O*-tosyl derivative [20] (XX) was formed from the ester (IX). Structure (XVII) was confirmed by acid hydrolysis of the ester (XIX) to syrupy methyl 2-*O*-tosyl-α-D-galactoside [21] (XXII) which gave the known crystalline 4 : 6-*O*-benzylidene compound [21,22] (XXIII). Hydrolysis of the glycoside (XXIII) yielded methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-taloside (XXIV) identified by comparison with an authentic sample.

The guloside presented more difficulty. The methyl *O*-acetyl-*O*-*iso*propylidene-α-D-guloside, m. p. 177—179°, described by the earlier workers could not be isolated; instead, the product had m. p. 165—167°. Deacetylation gave a methyl *O*-*iso*propylidene-α-D-guloside with the same physical constants as that isolated by Oldham and Robertson; it consumed 1 mol. of periodate. The deacetylated gulose derivative must therefore be the cyclic 4 : 6-acetal (XXV). Toluene-*p*-sulphonylation of the acetyl compound gave a derivative of m. p. 128—129° and $[\alpha]_D$ +47·3°; Labaton and Newth report m. p. 122—123° and $[\alpha]_D$ +52·2° for their *O*-acetyl-*O*-tosyl derivative. It seemed likely that the *O*-acetyl compound of m. p. 177—179° previously isolated was isomeric with that described in this paper; attempts to cause acetyl migration have so far been unsuccessful. It was, however, certain that the guloside product was methyl 2(or 3)-*O*-acetyl-4 : 6-*O*-*iso*propylidene-α-D-guloside (VIII) or (XXVI); the corresponding tosyl compounds were (IX) or (XXVII).

While much is known regarding the formation of chlorohydrins from sugar epoxides, the reaction with anhydrous acetone has received little attention. The problem remains as to the origin of each *iso*propylidene derivative in Oldham and Robertson's work.

[16] Harvey, Michalski, and Todd, *J.*, 1951, 2271.
[17] Baddiley, Buchanan, and Szabó, *J.*, 1954, 3826.
[18] Iselin and Reichstein, *Helv. Chim. Acta*, 1946, **29**, 508.
[19] Ohle and Thiel, *Ber.*, 1933, **66**, 525.
[20] Rao and Smith, *J.*, 1944, 229.
[21] Wiggins, *J.*, 1944, 522.
[22] Reber and Reichstein, *Helv. Chim. Acta*, 1945, **28**, 1164.

Preliminary experiments indicate that the guloside is derived from the 3 : 4-anhydrogalactoside, and experiments on this point will be reported later.




Scheme II.

## Experimental

*Methyl* 4 : 6-O-*Benzylidene*-α-D-*galactoside*.—This compound, required in the preparation of the 2 : 3-anhydroguloside (XV), was made by Reichstein and Sorkin's method [15] from methyl α-D-galactoside of $[\alpha]_D$ +195° which had been purified through the tetra-acetate. It had m. p. 168—170° and $[\alpha]_D^{23}$ +141·3° (*c* 3·11 in $CHCl_3$), in agreement with Bell and Greville [23] who give m. p. 169—170° and $[\alpha]_D$ +144° (in $CHCl_3$).

*Methyl* 2-*Chloro*-2-*deoxy*-α-D-*idoside*.—Methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-guloside (m. p. 175—175·5°; 1·5 g.) was heated under reflux in acetone (170 c.c.) containing 2N-hydrochloric acid (4·5 c.c.) for 4 hr. The solution was neutralised with lead carbonate, filtered, and evaporated to dryness. Extraction of the solid residue with hot ethyl acetate followed by evaporation left a syrup which crystallised. Recrystallised from ethyl acetate the chlorodeoxy-idoside (0·5 g., 42%) had m. p. 124—126°, $[\alpha]_D^{22}$ +86·8° (*c* 0·34 in $H_2O$) {Labaton and Newth give m. p. 124—126°, $[\alpha]_D^{18}$ +84° (in $H_2O$)} (Found: C, 39·4; H, 6·2; Cl, 16·8; OMe, 14·9. Calc. for $C_7H_{13}O_5Cl$: C, 39·5; H, 6·1; Cl, 16·7; OMe, 14·6%). When treated with aqueous sodium metaperiodate, the glycoside consumed 0·92 mol. (3 hr.); 0·97 mol. (5 hr.); 1·22 mol. (24 hr.). The initial preparation of this compound had m. p. 111—112°, but yielded the material of m. p. 124—126° by inoculation of the melt at 120°.

*Methyl* 4 : 6-O-*Benzylidene*-2-*chloro*-2-*deoxy*-α-D-*idoside*.—(i) Prepared by Labaton and Newth's method,[2] the compound had m. p. 166°, $[\alpha]_D^{20}$ +64·8° (*c* 1·80 in $CHCl_3$) (Found: C, 56·3; H, 6·1; OMe, 10·8. Calc. for $C_{14}H_{17}O_5Cl$: C, 55·9; H, 5·7; OMe, 10·3%). Labaton and Newth give m. p. 166°, $[\alpha]_D^{18}$ +67·2° (in $CHCl_3$). (ii) Prepared (85% yield) by treatment of methyl 2-chloro-2-deoxy-α-D-idoside (from the anhydroguloside above) with benzaldehyde and zinc chloride, and crystallised from ethanol, it had m. p. and mixed m. p. 166° and $[\alpha]_D^{20}$ +65·6° (*c* 1·85 in $CHCl_3$) (Found: C, 56·0; H, 5·9; OMe, 9·8%).

[23] Bell and Greville, *J.*, 1955, 1136.

*Action of Sodium Methoxide on Methyl* 4 : 6-O-*Benzylidene*-2-*chloro*-2-*deoxy*-α-D-*idoside*.—The glycoside (0·25 g.) was dissolved in methanol (5 c.c.) containing sodium methoxide (from 0·05 g. of sodium) by gentle heating. Within a few minutes the anhydro-sugar separated as fine needles. After 10 hr., water (5 c.c.) was added; the anhydro-sugar was filtered off and washed with water. The product (yield quantitative) had m. p. 175—175·5°, $[\alpha]_D^{20}$ −6·5° (*c* 1·14 in $CHCl_3$) (Found: C, 63·6; H, 6·2; OMe, 12·3. Calc. for $C_{14}H_{16}O_5$: C, 63·6; H, 6·1; OMe, 11·7%). Reichstein and Sorkin [16] give m. p. 178—179° (corr.) and $[\alpha]_D^{14}$ −7·4° (in $CHCl_3$) for methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-guloside. The m. p. was not depressed on admixture with an authentic sample, m. p. 175—175·5°.

*Methyl* 4-*Chloro*-4-*deoxy*-α-D-*glucoside*.—Prepared according to directions of Labaton and Newth,[2] the glycoside had m. p. 114—115°, $[\alpha]_D^{21}$ +130·9° (*c* 1·03 in $H_2O$) (Found: C, 39·3; H, 6·2. Calc. for $C_7H_{13}O_5Cl$: C, 39·5; H, 6·1%). Labaton and Newth give m. p. 113—114°, $[\alpha]_D^{18}$ +138·3° (in $H_2O$). It consumed 0·42 mol. of sodium periodate after 20 hr.; 0·58 (40 hr.); 1·03 (170 hr.); 1·06 (212 hr.).

*Treatment of the Methyl* O-*Acetylanhydro*-6-O-*triphenylmethyl*-α-D-*hexoside Mixture with Hydrogen Chloride in Acetone*.—The mixture of anhydro-sugars was prepared from methyl 2 : 3-di-*O*-benzoyl-4-*O*-tosyl-6-*O*-triphenylmethyl-α-D-glucoside (18·5 g.) by Oldham and Robertson's method.[1] A solution of dry hydrogen chloride (3 g.) in acetone (50 c.c.) was added to a solution of the anhydro-sugar in acetone (50 c.c.), and the mixture left for 1 hr. at room temperature. Anhydrous sodium carbonate (40 g.) was added and after a few minutes' shaking the solid was filtered off. The filtrate was evaporated to small volume and then poured into an excess of water containing a little pyridine. When the triphenylmethanol had crystallised it was removed and the filtrate extracted several times with chloroform. The combined extracts were washed with dilute sulphuric acid and water, dried ($Na_2SO_4$), and evaporated to dryness. On treatment with ether *methyl* O-*acetyl*-4 : 6-O-iso*propylidene*-α-D-*guloside* (0·95 g.), m. p. 164—166°, separated. Recrystallised from ethanol or ethyl acetate this had m. p. 165—167°, $[\alpha]_D^{21}$ +75·6° (*c* 0·73 in $CHCl_3$) (Found: C, 52·5; H, 7·6. $C_{12}H_{20}O_7$ requires C, 52·2; H, 7·2%). The same product was obtained, in slightly higher yield, when the acetone solutions were mixed at 0°, or when the chloroform solution was not shaken with acid. Contact with the sodium carbonate overnight merely lowered the yield slightly.

To the ethereal mother-liquor light petroleum (b. p. 60—80°; 2 vols.) was added and the solution left for 24 hr. The crystalline solid, m. p. 95—99°, was recrystallised from ether–light petroleum (b. p. 60—80°), to give methyl 6-*O*-acetyl-3 : 4-*O*-*iso*propylidene-α-D-galactoside (0·7 g.), m. p. 101—102°, $[\alpha]_D^{17}$ +126·0° (*c* 1·51 in $CHCl_3$) (Found: C, 52·1; H, 7·4. Calc. for $C_{12}H_{20}O_7$: C, 52·5; H, 7·2%). Oldham and Robertson [1] give m. p. 101—102° and $[\alpha]_D$ +127·3° (in $CHCl_3$); Labaton and Newth [2] give m. p. 101—102° and $[\alpha]_D$ +122·4° (in $CHCl_3$).

The aqueous liquor was freed from halide ion by silver carbonate, followed by hydrogen sulphide, and evaporated to dryness. Paper chromatography showed the presence of methyl mono-*O*-acetyl-guloside and -galactoside.

*Methyl* 6-O-*Acetyl*-3 : 4-iso*propylidene*-2-O-*tosyl*-α-D-*galactoside*.—Methyl 6-*O*-acetyl-3 : 4-*iso*propylidene-α-D-galactoside (0·50 g.) was treated with toluene-*p*-sulphonyl chloride (1 g.) in pyridine (5 c.c.) for 24 hr. After destruction of the excess of acid chloride the mixture was poured into water, and the *product* filtered off and washed with water. Recrystallisation from light petroleum (b. p. 60—80°) gave needles (0·50 g.), m. p. 107—107·5°, $[\alpha]_D^{17}$ +146·9° (*c* 1·22 in $CHCl_3$) (Found: C, 53·0; H, 6·3; S, 7·7. $C_{19}H_{26}O_9S$ requires C, 53·0; H, 6·0; S, 7·4%).

*Methyl* 3 : 4-O-iso*Propylidene*-2-O-*tosyl*-α-D-*galactoside*.—The above sugar (0·39 g.) was deacetylated with sodium methoxide in methanol. Solid carbon dioxide was added, the solution evaporated to dryness, and the solid extracted with hot benzene. The extract was evaporated to dryness. The *product*, crystallised from benzene–light petroleum (b. p. 60—80°), gave needles (0·31 g.), m. p. 162°, $[\alpha]_D^{19}$ +153·1° (*c* 1·53 in $CHCl_3$) (Found: C, 52·4; H, 6·4; S, 8·4. $C_{17}H_{24}O_8S$ requires C, 52·6; H, 6·2; S, 8·3%).

*Methyl* 3 : 4-O-iso*Propylidene*-2 : 6-*di*-O-*tosyl*-α-D-*galactoside*.—The above sugar (0·2 g.) was treated with toluene-*p*-sulphonyl chloride (1 g.) in pyridine (5 c.c.). The product, isolated in the usual way and crystallised from chloroform–light petroleum (b. p. 40—60°) (0·2 g.), had m. p. 151°, $[\alpha]_D^{21}$ +115·3° (*c* 1·32 in $CHCl_3$). Iselin and Reichstein [16] give m. p. 149—150°, $[\alpha]_D$ +113·5° (in $CHCl_3$). An authentic sample (m. p. 151°) gave no m. p. depression on admixture, and had an identical infrared spectrum (KBr disc) (Found: C, 52·8; H, 5·7. Calc. for $C_{24}H_{30}O_{10}S_2$: C, 53·1; H, 5·5%).

XUM

*Methyl* 4 : 6-O-*Benzylidene*-2-O-*tosyl*-α-D-*galactoside*.—Methyl 3 : 4-*O*-*iso*propylidene-2-*O*-tosyl-α-D-galactoside (0·7 g.) was heated with 2N-acetic acid (30 c.c.) under reflux for 1 hr. The solution was evaporated to dryness and the syrupy residue shaken with benzaldehyde (15 c.c.) and powdered zinc chloride (2 g.) at room temperature for 20 hr. Water and chloroform were added and the chloroform layer was steam-distilled until benzaldehyde had been removed. Sodium hydrogen carbonate was added and the solution extracted with chloroform. Evaporation of the chloroform layer left a solid which crystallised when triturated with ether and light petroleum. Recrystallised from acetone–ether–light petroleum (b. p. 60—80°) the product (0·52 g., 66%) had m. p. 134—134·5°, $[\alpha]_D^{21}$ +121·6° (*c* 1·66 in $CHCl_3$) (Found: C, 58·1; H, 5·9. Calc. for $C_{21}H_{24}O_8S$: C, 57·8; H, 5·5%). Reber and Reichstein [22] gave m. p. 137—138° and 187—188° and $[\alpha]_D^{15}$ +116·6° (in $CHCl_3$); Wiggins [21] gave m. p. 179—180° and $[\alpha]_D^{18}$ +117·8° (in $CHCl_3$).

*Methyl* 2 : 3-*Anhydro*-4 : 6-O-*benzylidene*-α-D-*taloside*.—The above sugar was treated with sodium methoxide in methanol (cf. Reber and Reichstein [22]). The product had m. p. 234—236° alone or in admixture with an authentic sample (m. p. 234—236°); Reichstein and Sorkin [15] give m. p. 241—242° (corr.). The infrared spectra were also identical.

*Methyl* 4 : 6-O-iso*Propylidene*-α-D-*guloside*.—The preceding monoacetyl derivative was deacetylated with sodium methoxide in methanol. The product crystallised from ethyl acetate–light petroleum (b. p. 40—60°) as needles, m. p. 132—134°, $[\alpha]_D^{20}$ +88·9° (*c* 1·77 in $CHCl_3$) (Found: C, 51·1; H, 7·6. Calc. for $C_{10}H_{18}O_6$: C, 51·3; H, 7·7%). Oldham and Robertson [1] give m. p. 132—133°, $[\alpha]_D$ +88·5° (in $CHCl_3$). The glycoside consumed 1·00 mol. of sodium periodate in 2 hr. (constant value).

*Methyl* O-*Acetyl*-4 : 6-O-iso*propylidene*-O-*tosyl*-α-D-*guloside*.—The preceding acetyl derivative (0·88 g.) was treated in pyridine (10 c.c.) with toluene-*p*-sulphonyl chloride (1 g.) for 36 hr. Isolation in the usual way gave the *derivative* (1·10 g., 80%), m. p. 124—126°. Recrystallisation from ethanol gave prisms, m. p. 128—129°, $[\alpha]_D^{21}$ +47·3° (*c* 2·08 in $CHCl_3$) (Found: C, 52·9; H, 6·3. $C_{19}H_{26}O_9S$ requires C, 53·0; H, 6·0%).

I thank Professor J. Baddiley, Dr. D. J. Bell, Dr. E. E. Percival, and Dr. J. C. P. Schwarz for helpful discussion, Professor M. Stacey, F.R.S., for a gift of methyl α-D-guloside, and the Department of Scientific and Industrial Research for financial support during part of this work.

LISTER INSTITUTE OF PREVENTIVE MEDICINE, LONDON, S.W.1.
KING'S COLLEGE, NEWCASTLE UPON TYNE. [*Received, September 23rd*, 1957.]

---

## 200. *The Separation and Characterisation of the 2′ : 5′- and 3′ : 5′-Diphosphate and the 2′ : 3′ : 5′-Triphosphate of Adenosine.*

By J. BADDILEY, J. G. BUCHANAN, and R. LETTERS.

The 2′ : 5′- and 3′ : 5′-diphosphate of adenosine have been separated from each other by paper chromatography and by ion-exchange chromatography, employing concave gradient elution with calcium chloride and hydrochloric acid. The phosphates were characterised by enzymic and chemical hydrolysis.

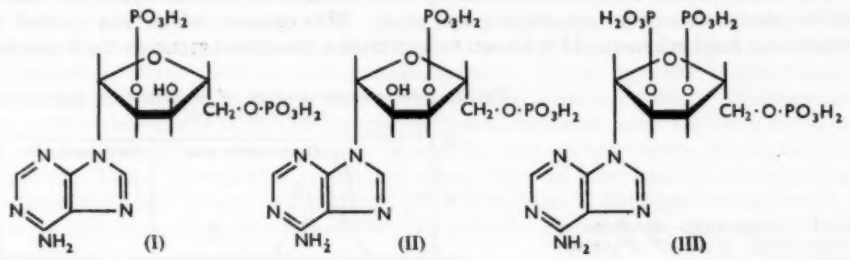
The value of hydrolysis at pH 4 for the location of phosphate groups in polyphosphates is discussed.

Adenosine-2′ : 3′ : 5′ triphosphate has been prepared by phosphorylation of adenosine with an excess of dibenzyl phosphorochloridate, followed by removal of protecting groups. The action of phosphatases on this ester has been studied.

THE isomeric diphosphates of adenosine are important structural units in several nucleotide coenzymes. The adenosine-2′ : 5′ diphosphate (I) structure occurs in triphosphopyridine nucleotide, whereas the isomeric 3′ : 5′-diphosphate (II) is a component of coenzyme A and "active sulphate". Although unequivocal syntheses of these diphosphates have not been achieved, their structures have been established by enzymic methods.[1] A mixture

[1] Wang, Shuster, and Kaplan, *J. Biol. Chem.*, 1954, **206**, 299.

containing the two isomers has been obtained by phosphorylation of adenosine with an excess of dibenzyl phosphorochloridate followed by removal of benzyl groups.[2] Todd and his collaborators were unable to resolve this mixture, but its value in the synthesis of certain nucleotide coenzymes was indicated. It was suggested that most of the known methods for the synthesis of pyrophosphates from such a phosphate would inevitably cause migration of the phosphate at the 2′- or 3′-position, and subsequent steps would always produce a mixture of phosphates.




In a recent synthesis of "active sulphate" (adenosine 3′-phosphate 5′-sulphatophosphate) we showed that adenosine-3′ : 5′ diphosphate (II) (isolated from natural sources) reacts with the pyridine–sulphur trioxide complex in a buffer solution to give the desired 3′-phosphate 5′-sulphatophosphate.[3] Although some cyclisation of the phosphate at the 3′-position occurred the two products were separated from each other quite readily by paper chromatography or by electrophoresis. It is unlikely that phosphate migration would occur in such a synthesis. It follows therefore that a laboratory-scale separation of the isomeric diphosphates of adenosine, although it may present great difficulty, would be of value for synthetic work. Such a separation would also provide an alternative to the enzymic identification of these compounds in studies on the structure of nucleotide coenzymes.

A method has been developed in these laboratories for the resolution of complex mixtures of nucleotides by ion-exchange chromatography on Dowex-1 resin of low cross-linkage, employing an eluting solution of calcium chloride in an apparatus which ensures a continuous, concave concentration gradient.[4] This method, which is particularly effective in the separation of the more acidic nucleotides, has the additional advantage of ease of isolation of the pure products. Evaporation of solvent from the eluate, and addition of an alcohol–ether mixture to the residue, yields the calcium salts of the nucleotides as insoluble precipitates. The technique has now been applied successfully to the separation and isolation of the isomeric adenosine diphosphates.

The synthesis of the mixed diphosphates was carried out by a method similar to that used by the Cambridge workers, and we are grateful to them for information in advance of publication. They found it necessary to remove benzyl groups and destroy cyclic phosphates in the neutral ester mixture in three separate operations, first by anionic debenzylation with lithium chloride, then by catalytic hydrogenolysis, and finally by alkaline hydrolysis. We have confirmed this observation and simplified the preparation by reversal of the last two stages. In this way the hydrogenolysis occurs more smoothly.

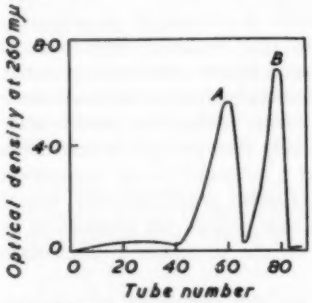
Separation of products was first attempted by chromatography on Dowex-2 resin in the formate form, resolution being achieved by concave gradient elution with ammonium formate. The 2′ : 5′- and the 3′ : 5′-diphosphate were not completely separated from each other by this method and reproducibility was not good. Excellent separation

[2] Cramer, Kenner, Hughes, and Todd, *J.*, 1957, 3297.
[3] Baddiley, Buchanan, and Letters, *Proc. Chem. Soc.*, 1957, 147.
[4] Pontis and Blumsom, in the press.

occurred (see Fig. 1) on the chloride form of Dowex-1, by concave gradient elution with a solution of calcium chloride and hydrochloric acid. A concentration range from 0·03M-calcium chloride and 0·0045N-hydrochloric acid, up to 0·07M and 0·007N respectively, was chosen. The diphosphates were isolated from appropriate fractions as their calcium salts. Adenosine-2′ : 5′ diphosphate was eluted from the column in advance of the 3′ : 5′-diphosphate. This was in agreement with the order of elution of monophosphates of adenosine, where the 2′-phosphate precedes the 3′-phosphate.[5]

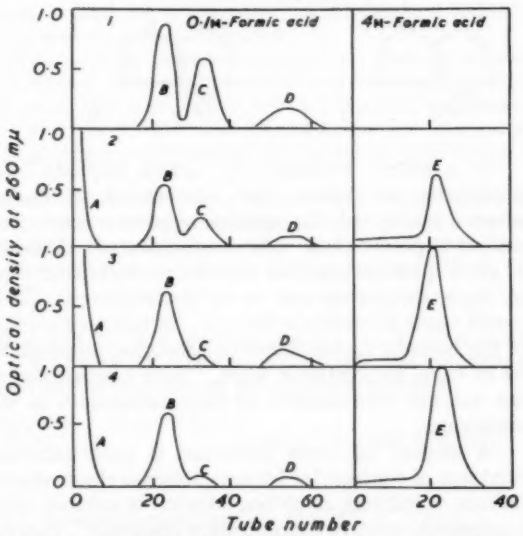
The diphosphates were characterised by their behaviour towards hydrolysis with a specific phosphatase from germinating rye grass. This enzyme, which was purified by Shuster and Kaplan's method,[6] is known to hydrolyse a phosphate group at the 3′-position

FIG. 1. *Ion-exchange separation of adenosine-2′ : 5′ and -3′ : 5′ diphosphates.*




*A, Adenosine-2′ : 5′ diphosphate.*
*B, Adenosine-3′ : 5′ diphosphate.*

FIG. 2. *Ion-exchange analysis of products from hydrolysis of nucleotides at* pH 4.




*1, Authentic nucleotides for calibration of column. 2, Hydrolysate of adenosine-2′ : 5′ diphosphate. 3, Hydrolysate of adenosine-3′ : 5′ diphosphate. 4, Hydrolysate of adenosine-2′ : 3′ : 5′ triphosphate.*
*A, Adenosine. B, Adenosine-5′ phosphate. C, Adenosine-2′ phosphate. D, Adenosine-3′ phosphate. E, Adenosine diphosphates.*

in adenosine and its phosphates, but is without action on phosphate groups in other positions. In accordance with the earlier observations, it was shown that adenosine-3′ : 5′ diphosphate (II) was readily hydrolysed by this enzyme to adenosine-5′ phosphate and inorganic phosphate, whereas the 2′ : 5′-diphosphate (I) was unaffected (see Table 1). Our enzyme preparation contained a trace of a nucleoside-5′ phosphatase, and consequently a very small amount of hydrolysis of the adenosine-5′ phosphate, liberated from the 3′ : 5′-diphosphate, was observed.

An alternative proof of structure of the diphosphates was obtained by partial hydrolysis at pH 4. The mechanism of phosphate hydrolysis at this pH differs from that in stronger acid and is known to involve phosphorus–oxygen fission.[7] It follows that hydrolysis at

[5] Cohn, *J. Amer. Chem. Soc.*, 1949, **71**, 2285.
[6] Shuster and Kaplan, *J. Biol. Chem.*, 1953, **201**, 535.
[7] Desjobert, *Compt. rend.*, 1947, **224**, 575; *Bull. Soc. chim. France*, 1947, **14**, 809; Butcher and Westheimer, *J. Amer. Chem. Soc.*, 1955, **77**, 2420.

the higher pH, although quite rapid, should be accompanied by little or no phosphate migration even in those esters which contain an adjacent hydroxyl group. The validity of these views is illustrated by the behaviour of glycerophosphates [8] and other polyol phosphates [9] towards hydrolysis at pH 4. In both cases removal of phosphate occurs readily without migration.

In order to evaluate hydrolysis at pH 4 as a method for determining the structure of nucleotides, controlled conditions were employed with the 2′- and 3′-phosphate of adenosine. After 4 hr. at 100° in an ammonium formate buffer (pH 4) the products from the two nucleotides were examined by ion-exchange chromatography. Previously calibrated columns were used under standard conditions for the separation and quantitative determination of the three isomeric monophosphates. These experiments (see Table 2) showed that substantial hydrolysis can be effected with little migration. Approximately 46% of the adenosine-3′ phosphate was hydrolysed to adenosine, only 4% being converted into the 2′-phosphate. Adenosine-2′ phosphate was slightly more labile than the 3′-isomer. Under comparable conditions about 52% of this isomer was hydrolysed to adenosine, and 7% was converted into the 3′-phosphate. Although the differences in rates of hydrolysis and migration of the two isomers are not large, they are probably significant.

This method of analysis was applied to hydrolysates of adenosine-2′ : 5′ and -3′ : 5′ diphosphate. The results (Table 2, Fig. 2) show that phosphate groups at positions 2′ and 3′ are more labile than that at 5′. Slight migration of phosphate between the 2′- and 3′-position was observed, and it is noteworthy that migration from 2′ to 3′ is somewhat greater than that in the reverse direction. The amount of migration which occurs at pH 4 is slight in all cases and in no way invalidates structural determinations based on such hydrolyses. Adenosine-2′ : 5′ diphosphate gave adenosine-2′ and -5′ phosphate with a trace of the 3′-phosphate (about 3%). Similarly, the 3′ : 5′-diphosphate gave the 3′- and 5′-phosphate, and very little 2′-phosphate. No evidence was obtained for the presence of adenosine-2′ : 3′ diphosphate in the nucleoside diphosphate preparations under examination. It would be unnecessary normally to carry out an ion-exchange separation of products, since the characterisation of these nucleoside diphosphates can be effected rapidly and accurately from the qualitative information given by paper chromatography of the hydrolysates.

From the experiments on nucleotides described here, and from similar investigations on polyol phosphates, it seems that hydrolysis at pH 4 can be of considerable value in structural determination. The outstanding advantage of this over many other hydrolytic methods is the comparatively small amount, or even complete absence, of group migration. The ready hydrolysis of glycerophosphates and their derivatives at pH 4 has been known for a considerable time, and the absence of phosphate migration under these conditions is also well known. However, even in the phospholipid field, only occasional use has been made of these facts. It is interesting that, although no migration of the phosphate group was observed with ribitol 1(5)-phosphate at pH 4, a small amount of migration occurred under comparable conditions with adenosine-2′ and -3′ phosphate, and with the diphosphates. Migration was detectable even at pH 6 with these nucleotides. We conclude that the extremely favourable steric disposition of the phosphate and adjacent hydroxyl group in the ribofuranose ring of nucleotides accounts for these differences. It has been suggested that the conjugate acid which occurs as an intermediate in the hydrolysis of phosphoric esters in strongly acidic solution is also an intermediate in phosphate migration.[9,10] The small amount of phosphate migration which occurs with nucleotides at pH 4 may be related to the concentration of conjugate acid at that pH. It should be noted that the presence of a hydroxyl group in very close proximity to the

[8] Bailly, *Bull. Soc. chim. France*, 1942, **9**, 340.
[9] Baddiley, Buchanan, and Carss, *J.*, 1957, 4058.
[10] Brown, Magrath, Neilson, and Todd, *Nature*, 1956, **177** 1124.

phosphoric ester linkage is likely to enhance the amount, and modify the structure, of the conjugate acid present at relatively high pH values.

Todd and his collaborators [2] were unable to detect a triphosphate of adenosine in the mixture obtained by phosphorylation of the nucleoside with an excess of dibenzyl phosphorochloridate. In our hands, however, the method gave appreciable amounts of adenosine-2′ : 3′ : 5′ triphosphate (III). This compound was eluted from an ion-exchange column after the diphosphates, and had a lower $R_P$ than these on paper chromatograms run with basic solvent mixtures. It had an absorption maximum at 260 mμ and was deaminated with nitrous acid to inosine-2′ : 3′ : 5′ triphosphate. This demonstrated the absence of a phosphate group on the 6-amino-substituent of the adenine residue. The unlikely possibility of the presence of a 5′-pyrophosphate group was eliminated by the failure of *Crotalus atrox* venom pyrophosphatase to attack the triphosphate. The crude venom is known to hydrolyse pyrophosphates, and it has been shown that the 5′-phosphatase in a similar rattlesnake venom is without action on nucleoside-5′ phosphates which bear a substituent at the 2′- or 3′-position.[11] The triphosphate was also unaffected by the 3′-phosphatase from rye grass. It seems that substitution of all hydroxyl groups in the ribose residue of a nucleoside by phosphoric ester groups prevents the action of both 3′- and 5′-phosphatase.

The triphosphate was hydrolysed at pH 4 under conditions comparable to those used with the diphosphates. Paper chromatography showed that all the triphosphate had been hydrolysed. The principal products were the diphosphates and adenosine-5′ phosphate. Smaller amounts of adenosine-2′ and -3′ phosphate were detected; these were present in approximately equal proportion. Although quantitative results were not obtained, it is clear that the triphosphate is hydrolysed at pH 4 in the manner expected from the results described on the mono- and di-phosphates of adenosine.

## Experimental

*Adenosine-2′(3′) : 5′ Diphosphate and Adenosine-2′ : 3′ : 5′ Triphosphate.*—The method used is essentially that described by Cramer *et al.*[3] but with certain modifications.

Adenosine (5 g.; dried at 110°/1 mm.) was dissolved in boiling anhydrous pyridine (250 ml.). The solution was cooled to −40° (without solidifying) and added to dibenzyl phosphorochloridate (from 26 g. of dibenzyl phosphite). The mixture was allowed to warm slowly to 0°, and kept at this temperature for a further 18 hr. before addition of 2-ethoxyethanol (13 ml.). The pyridine hydrochloride, which had separated within 30 min., was collected and the filtrate was evaporated. After addition of 2-ethoxyethanol (50 ml.) and subsequent evaporation, the syrup was dissolved in ethoxyethanol (100 ml.) containing anhydrous lithium chloride (12 g.), and kept at 100° for 3 hr. with exclusion of moisture. Addition of ether (500 ml.) to the cooled solution precipitated a gum which solidified when shaken with ethanolic acetone, a cream-coloured powder (12·6 g.) being obtained. The solid was treated with N-sodium hydroxide (300 ml.) at room temperature. After 40 hr. the solution was neutralised to pH 7 with dilute hydrochloric acid, extracted with ether (2 × 50 ml.) and concentrated to 150 ml. The solution was passed through a column (20 × 5 cm.) of Dowex-50-(× 8) resin (lithium form), which was washed with water. When no more light-absorbing (at 260 mμ) material was eluted, the solution was evaporated. The residual syrup was shaken with a mixture of acetone (400 ml.) and ethanol (100 ml.), and the resulting solid was collected by centrifugation. It was washed with a second portion of ethanolic acetone, then dried. The solid (8·7 g.) was dissolved in water (150 ml.), acetic acid (2 ml.) added, and the solution hydrogenated with palladium black (from 0·2 g. of palladium chloride). After removal of catalyst, the solution [containing 3·86 g. of nucleotides calculated as adenosine-2′(3′) : 5′ diphosphate, based on optical density at 260 mμ] was passed through a column (20 × 5 cm.) of Dowex-2-(× 10) resin (chloride form) and the column was washed with water (1 l.). Monophosphates were removed by passing a solution of

[11] Kornberg and Pricer, *J. Biol. Chem.*, 1950, **186**, 557.

0·003N-hydrochloric acid (2 l.) through the column; 0·025N-acid (4 l.) removed the adenosine-2′(3′) : 5′ diphosphate. Adenosine-2′ : 3′ : 5′ triphosphate was removed (in 1·5 l.) with 0·05N-hydrochloric acid which was 0·2N with respect to calcium chloride. The solution of adenosine-2′ : 3′ : 5′ triphosphate was adjusted to pH 7 with a suspension of calcium hydroxide, evaporated to 20 ml., and freeze-dried. The resulting solid was washed with alcoholic ether (3 × 50 ml.; 1 : 1) and finally with ether (3 × 50 ml.) until free from chloride. The residue (0·8 g.) was centrifuged and dried. It was dissolved in water (50 ml.) and passed through a column (10 × 3·2 cm.) of Dowex-50-(× 8) resin (hydrogen form), which was washed with water (1 l. until the eluate was free from light-absorbing (260 mμ) material. The eluate was freeze-dried and the residue redissolved in water (5 ml.). Addition of dry acetone (50 ml.) gave a white precipitate (300 mg.) of *adenosine-2′ : 3′ : 5′ triphosphate*, $\lambda_{max.}$ 257—258 mμ (ε 14,850) (Found: C, 22·4; H, 3·7; P, 17·5. $C_{10}H_{16}O_{13}N_5P_3,2H_2O$ requires C, 22·2; H, 3·7; P, 17·1%). The adenosine-2′(3′) : 5′ diphosphate (2·1 g.) was isolated in a similar manner and compared with an authentic specimen (kindly provided by Dr. G. W. Kenner) by paper chromatography and paper electrophoresis.

*Inosine-2′ : 3′ : 5′ Triphosphate.*—Adenosine-2′ : 3′ : 5′ triphosphate (25 mg.) was dissolved in 2N-acetic acid (10 ml.), and a solution of sodium nitrite (1 g.) in water (4 ml.) was added dropwise. After 36 hr. at room temperature the mixture was adjusted to pH 7 with 2N-sodium hydroxide, and barium acetate (50 mg.) was added. The *barium salt* of inosine-2′ : 3′ : 5′ triphosphate (35 mg.) was collected by centrifugation, washed with a small amount of water, and dried (Found: P, 9·5. $C_{10}H_{15}O_{14}N_4P_3Ba_3$ requires P, 9·9%). The barium salt had $\lambda_{max.}$ 249 mμ (ε 10,850) and $\lambda_{min.}$ 224 mμ (ε 3570) at pH 7·5. This spectrum corresponded closely with that reported for inosine [12] [$\lambda_{max.}$ 248·5 mμ (ε 12,250) and $\lambda_{min.}$ 223 mμ (ε 3400) at pH 6]. The inosine-2′ : 3′ : 5′ triphosphate was also characterised by paper electrophoresis (see Table 4).

*Separation of Adenosine-2′ : 5′ Diphosphate and Adenosine-3′ : 5′ Diphosphate.*—(a) *Formate system at* pH 4. A mixture of the isomeric diphosphates (15 mg.) was absorbed on a column (45 × 1·2 cm.) of Dowex-2-(× 10) resin (formate form; 200—400 mesh). Elution was carried out with ammonium formate solution (pH 4) in an apparatus designed to give a concave concentration–volume gradient. The concentration range was from 1·5M- to 3M-ammonium formate. The isomeric diphosphates were not completely separated in this sytem, but paper chromatography showed that adenosine-2′ : 5′ diphosphate was eluted before adenosine-3′ : 5′ diphosphate.

(b) *Chloride system.* Adenosine-2′(3′) : 5′ diphosphate (40 mg.) was adsorbed on a column (60 × 1·05 cm.) of Dowex-1-(× 2) resin (chloride form; 200—400 mesh) which was then washed with water (100 ml.). Elution was carried out with calcium chloride and hydrochloric acid solutions, in an apparatus which gave a concave concentration–volume gradient, similar to that used in (a). The concentration range was from 0·03M-calcium chloride and 0·0045N-hydrochloric acid, to 0·07M-calcium chloride and 0·007N-hydrochloric acid. The isomeric nucleotides were completely separated by this system, adenosine-2′ : 5′ diphosphate being eluted first from the column. The solutions of the nucleotides were adjusted to pH 7 with a suspension of calcium hydroxide, and the calcium salts were isolated as previously described. The elution diagrams are shown in Fig. 1. The *calcium salt* (26 mg.) of adenosine-2′ : 5′ diphosphate had $\lambda_{max.}$ 258 mμ (ε 14,250) and $\lambda_{min.}$ 227 mμ (ε 2875) (Found: C, 18·9; H, 4·2; P, 9·2. $C_{10}H_{11}O_{10}N_5P_2Ca_2,8H_2O$ requires C, 18·7; H, 4·2; P, 9·6%). The *calcium salt* (19 mg.) of adenosine-3′ : 5′ diphosphate had $\lambda_{max.}$ 258 mμ (ε 14,050) and $\lambda_{min.}$ 227 mμ (ε 2850) (Found: C, 20·8; H, 3·2; P, 9·9. $C_{10}H_{11}O_{10}N_5P_2Ca_2,5H_2O$ requires C, 20·3; H, 3·55; P, 10·5%).

*Action of Rye Grass Enzyme on Adenosine Phosphates.*—Rye grass enzyme was prepared by Shuster and Kaplan's method [6] and purified by ammonium sulphate precipitation and adsorption on $C_\gamma$ alumina. The action of the enzyme on the various nucleotides was determined, the following system being used: the nucleotide (0·4 mol.) in tri(hydroxymethylamino)methane buffer (0·2 ml.) at pH 7·5 was incubated overnight with enzyme solution (0·04 ml.) at 37°. The reaction was stopped by the addition of 20% trichloroacetic acid solution (0·2 ml.), and inorganic phosphate was determined by Fiske and Subbarow's method.[13] Control experiments were carried out on the same system to which trichloroacetic acid solution had been added at zero time. An experiment with adenosine-5′ phosphate indicated that a 5′-nucleotidase was

[12] Chargaff and Davidson, "Nucleic Acids," Academic Press, New York, Vol. I, p. 508.
[13] Fiske and Subbarow, *J. Biol. Chem.*, 1925, **66**, 375.

XUM

present in the purified preparation. The results of the enzyme experiments are shown in Table 1.

TABLE 1. *Enzymic hydrolysis of adenosine phosphates.*

| Substrate | Mols. of phosphate liberated per mol. of nucleotide | Hydrolysis (% of total phosphate) |
|---|---|---|
| Adenosine-5′ phosphate ..... | 0·15 | 15 |
| Adenosine-2′ phosphate ..... | 0 | 0 |
| Adenosine-3′ phosphate ..... | 0·95 | 95 |
| Adenosine-2′ : 5′ diphosphate ..... | 0 | 0 |
| Adenosine-3′ : 5′ diphosphate ..... | 1·13 | 56·5 |
| Adenosine-2′ : 3′ : 5′ triphosphate ..... | 0 | 0 |

*Action of* Crotalus atrox *Venom on Adenosine-2′ : 3′ : 5′ Triphosphate.*—Adenosine-2′ : 3′ : 5′ triphosphate (0·4 mol.) in a 0·25M-glycine–ammonia buffer (0·2 ml.; pH 9) was kept at 37° overnight. No inorganic phosphate was liberated. Under the same conditions, 1 mol. and 2 mols. of inorganic phosphate were liberated from adenosine-5′ phosphate and -5′ pyrophosphate respectively.

*Anion-exchange Analyses.*—In the following experiments a column (7·3 × 1·05 cm.) of Dowex-1-(× 2) resin (formate form; 200—400 mesh) was used with a flow rate of 0·3—0·5 ml./min. The same column was used throughout the investigation, without any apparent change in its adsorption characteristics. The adenosine monophosphates were eluted with 0·1N-formic acid, and the adenosine diphosphates with 4N-formic acid. Fractions (5 ml.) were collected by means of an automatic fraction collector. Nucleotides were determined quantitatively from the absorption of their solutions at 260 mμ.

*Hydrolysis of Adenosine Phosphates at* pH 4.—The nucleotide sample (2—3 mg.) was heated at 100° for 4 hr. with 0·4M-ammonium formate buffer (0·3 ml.; pH 4). Paper chromatographic examination of the hydrolysate with solvent systems A and B established the nature of the reaction products. Identification was confirmed and yields were determined by ion-exchange chromatography on a Dowex-1 column prepared in the above manner. The hydrolysis mixture was adjusted to pH 7·5 with N-ammonia and run on the column. Adenosine was recovered by washing the column with water (2 × 3 ml.) and nucleotides were eluted as described above. Results are given in Table 2 and Fig. 2.

TABLE 2. *Hydrolysis of adenosine phosphates at* pH 4.

| | | Nucleotide recovered (%) as | | | |
|---|---|---|---|---|---|
| | Hydrolysis to adenosine (%) | 2′-phosphate | 3′-phosphate | 5′-phosphate | diphosphates |
| Adenosine-2′ phosphate ..... | 52 | 41 | 7 | — | — |
| Adenosine-3′ phosphate ..... | 46 | 4 | 50 | — | — |
| Adenosine-2′ : 5′ diphosphate ... | 18 | 13·3 | 3·1 | 25·5 | 38 |
| Adenosine-3′ : 5′ diphosphate ... | 23·5 | 1 | 7 | 28 | 40 |
| Adenosine-2′ : 3′ : 5′ triphosphate | 21·5 | 2·2 | 2·8 | 23·5 | 50 |

*Paper Chromatography.*—Ascending-front chromatography was carried out on Whatman No. 4 paper, previously washed with 2N-acetic acid. The following solvent systems were used: (A) *n*-propyl alcohol–ammonia (*d* 0·88)–water (11 : 7 : 2); (B) saturated ammonium sulphate–0·1M-ammonium acetate–*iso*propyl alcohol [14] (79 : 19 : 2). Nucleotides were located by

TABLE 3. *Paper chromatography of nucleotides.*

| | $R_P$ in solvent A | $R_P$ in solvent B | | $R_P$ in solvent A | $R_P$ in solvent B |
|---|---|---|---|---|---|
| Adenosine ..... | 0·92 | 0·22 | Adenosine-3′ : 5′ diphosphate ..... | 0·29 | 0·50 |
| Adenosine-5′ phosphate ..... | 0·42 | 0·43 | Adenosine-2′ : 3′ : 5′ triphosphate | 0·14 | — |
| Adenosine-2′ phosphate ..... | 0·51 | 0·39 | Inorganic phosphate ..... | 0·38 | — |
| Adenosine-3′ phosphate ..... | 0·51 | 0·29 | Inosine-2′ : 3′ : 5′ triphosphate ... | 0·12 | — |
| Adenosine-2′ : 5′ diphosphate ..... | 0·29 | 0·57 | | | |

inspection under ultraviolet light and by the perchloric acid–molybdate spray reagent. $R_P$ values are shown in Table 3.

[14] Markham and Smith, *Biochem. J.*, 1951, **49**, 401.

*Paper Electrophoresis.*—Electrophoresis was carried out for 16 hr. on Whatman No. 4 paper soaked in 0·1M-ammonium acetate buffer at pH 6, with a voltage gradient of 1 v per cm. and a current of 2·5 milliamps.

TABLE 4. *Electrophoresis of nucleotides.*

| | Distance moved towards anode (cm.) | | Distance moved towards anode (cm.) |
|---|---|---|---|
| Adenosine-5′ phosphate ..... | 15 | Adenosine-2′ : 3′ : 5′ triphosphate | 47 |
| Adenosine-2′(3′) : 5′ diphosphate | 34 | Inosine-2′ : 3′ : 5′ triphosphate ... | 56 |

We thank the Council of King's College for the award of a Johnston Studentship and an Earl Grey Memorial Fellowship (to R. L.).

KING'S COLLEGE, UNIVERSITY OF DURHAM,
NEWCASTLE UPON TYNE.

[*Received, October 25th*, 1957.]

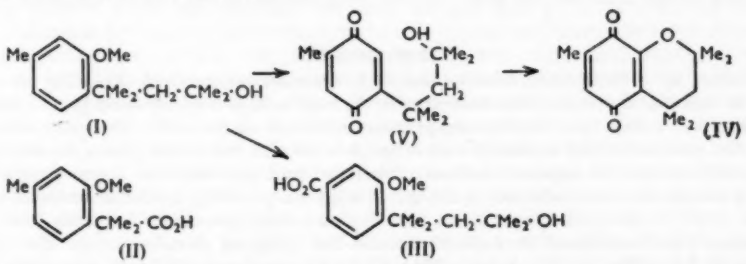
---

## 201. *An Anomalous Barbier–Wieland Degradation.*

By WILSON BAKER, R. F. CURTIS, J. F. W. MCOMIE, L. W. OLIVE, and V. ROGERS.

The tertiary alcohol (I) does not yield the normal Barbier–Wieland degradation product (II), but the acid (III) and the quinone (IV). The related tertiary alcohol (VI) gives a small yield of the expected acid (IX) and a little acetophenone, but the major reaction product is the ketone (VIII).

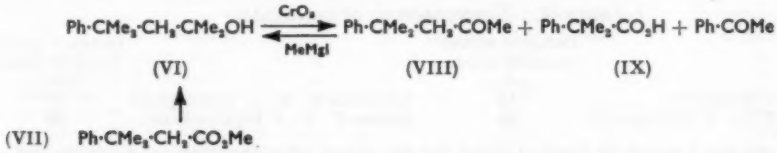
IT was reported by Baker, Curtis, and McOmie [1] that when the tertiary alcohol (I) was oxidised with chromic acid, the usual Barbier–Wieland degradation to the acid (II) did not occur, and they reserved further details and comment on this abnormal behaviour in a widely used degradative process.




When the alcohol (I) was oxidised with chromic acid in acetic acid–water, two products were isolated. The first (11·8%) was a carboxylic acid with the same number of carbon atoms as the alcohol (I), which could only arise by oxidation of a methyl group and must in consequence be regarded as 4-(4-carboxy-2-methoxyphenyl)-2 : 4-dimethylpentan-2-ol (III). The second product (9·0%) was a bright yellow, neutral, quinonoid substance which proved to be 2 : 2 : 4 : 4 : 7-pentamethylchroman-5 : 8-quinone (IV), this structure being based on the following facts. Reductive acetylation gave a colourless diacetyldihydro-compound, and a Zeisel estimation showed the absence of a methoxyl group, which must have been replaced by one of the quinonoid oxygen atoms. The infrared spectrum proved the absence of an alcoholic hydroxyl group and was compatible with the spectrum of a *p*-benzoquinone; [2,3] the spectrum is too complex to prove the existence of the ether linkage, though it is consistent with its presence. The colour suggests that the

[1] Baker, Curtis, and McOmie, *J.*, 1951, 77.
[2] Yates, Ardao, and Fieser, *J. Amer. Chem. Soc.*, 1956, **78**, 650.
[3] Otting and Staiger, *Chem. Ber.*, 1955, **88**, 828.

compound is a *para*-quinone rather than the possible isomeric *ortho*-quinone; the latter may also be excluded because *para*- but not *ortho*-quinones are formed by chromic acid oxidation of anisoles having free *ortho*- and *para*-positions.




It was considered of interest to study, under the same conditions, the Barbier–Wieland degradation of the simpler tertiary alcohol 2 : 4-dimethyl-4-phenylpentan-2-ol (VI), which possesses the same aliphatic chain but is without other substituents in the aromatic nucleus. The alcohol (VI) was prepared by reaction of methylmagnesium iodide with methyl β-methyl-β-phenylbutyrate (VII) or, more conveniently, with 4-methyl-4-phenylpentan-2-one (VIII). Oxidation of this alcohol with chromic acid in acetic acid–water at 60° gave three products: the normal degradation product, α-methyl-α-phenylpropionic acid (IX) (19%); 4-methyl-4-phenylpentan-2-one (VIII) (39%); and acetophenone (8%); the yields quoted are those before final purification. A similar oxidation at room temperature gave α-methyl-α-phenylpropionic acid (IX) (5%), 4-methyl-4-phenylpentan-2-one (60%), and acetophenone (2%). It is thus established that the failure of the tertiary alcohol (I) to undergo the usual degradation to the acid (II) cannot be ascribed solely to the steric effect of the groups attached to the quaternary carbon atom, but that it is primarily due to the presence of the methoxyl group which allows an oxidative attack on the aromatic nucleus, to give, first, the quinone (V) which undergoes reductive cyclisation with the tertiary hydroxyl group and then further oxidation to the quinone (IV).

Oxidation of *tert.*-butylbenzene with chromic acid in acetic acid–water gives trimethylacetic acid rather than benzoic acid, but the hydrocarbon is not readily oxidised.

## Experimental

*Oxidation of* 4-(2-*Methoxy*-4-*methylphenyl*)-2 : 4-*dimethylpentan*-2-*ol* (I).—The alcohol (I) (1·4 g.) in acetic acid (10 ml.) was treated with chromic acid (3·0 g.) in water (5 ml.) and acetic acid (10 ml.) at such a rate that the temperature remained at 30—40°. Next day the mixture was diluted with water and extracted with ether (3 × 50 ml.), the bright yellow ethereal solution shaken with excess of aqueous sodium carbonate, and the alkaline layer acidified. The resulting precipitate was collected (0·186 g., 11·8%; m. p. 200°), sublimed under diminished pressure (200°/11 mm.), and crystallised from benzene–light petroleum (b. p. 60—80°), giving 4-(4-*carboxy*-2-*methoxyphenyl*)-2 : 4-*dimethylpentan*-2-*ol* (III) as rhombs, m. p. 205° (Found: C, 68·1; H, 7·6; OMe, 11·5%; equiv., 261. $C_{15}H_{22}O_4$ requires C, 67·7; H, 8·3; OMe, 11·7%; equiv., 266).

The yellow ethereal solution was dried ($MgSO_4$) and yielded an oil from which bright yellow needles separated. These were collected, washed with ice-cold methanol, and crystallised from aqueous methanol, giving 2 : 2 : 4 : 4 : 7-*pentamethylchroman*-5 : 8-*quinone* (IV) as yellow needles (0·125 g., 9·0%), m. p. 111°; after recrystallisation from light petroleum (b. p. 40—60°) it had m. p. 112° (Found: C, 71·7; H, 7·7. $C_{14}H_{18}O_2$ requires C, 71·8; H, 7·7%).

Reductive acetylation of this quinone (IV) (0·100 g.) was carried out in acetic anhydride (5 ml.) and glacial acetic acid (1 ml.) under reflux by gradual addition of zinc dust until the yellow colour was discharged. After boiling for a further 2 hr., the whole was poured into water, the solid was collected and extracted with hot methanol (4 × 5 ml.), the extracts were concentrated and diluted with water, and the solid (0·109 g.) recrystallised from light petroleum (b. p. 40—60°), giving 5 : 8-*diacetoxy*-2 : 2 : 4 : 4 : 7-*pentamethylchroman* as colourless prisms, m. p. 95° (Found: C, 67·4; H, 7·6. $C_{18}H_{24}O_4$ requires C, 67·5; H, 7·5%).

2 : 4-*Dimethyl*-4-*phenylpentan*-2-*ol* (VI).—(*a*) Methyl β-methyl-β-phenylpropionate, b. p. 116—125°/11 mm., was prepared by esterification of the acid [4] by the Fischer–Speier method.

[4] Bergmann, Taubadel, and Weiss, *Ber.*, 1931, **64**, 1493.

This ester (6 g.; 1 mol.) in dry ether (30 ml.) was added slowly to an ethereal solution of methylmagnesium iodide (3 mols.) prepared from magnesium (2·25 g.), methyl iodide (13·2 g.), and ether (75 ml.), and the mixture was boiled for 12 hr., then poured into dilute hydrochloric acid and ice. The ethereal layer was shaken with aqueous sodium sulphite, the ether removed, and the residual oil boiled for 4 hr. with sodium hydroxide (1·5 g.) in water (7·5 ml.) and ethanol (30 ml.) to hydrolyse unchanged ester. Ether-extraction then yielded an oil, b. p. 74—79°/0·2 mm., b. p. 90—92°/0·5 mm. (4·7 g., 78%). At 0° this 2 : 4-*dimethyl*-4-*phenylpentan*-2-*ol* (VI) crystallised in plates, m. p. 24—26° (Found: C, 81·0; H, 10·1. $C_{13}H_{20}O$ requires C, 81·3; H, 10·4%).

(*b*) A solution of 4-methyl-4-phenylpentan-2-one (VIII) (30 g.) (prepared by condensation of benzene with mesityl oxide [5]) [the 2 : 4-*dinitrophenylhydrazone* separates from ethanol in yellow plates, m. p. 98·5° (Found: C, 60·5; H, 5·6; N, 16·0. $C_{18}H_{20}O_4N_4$ requires C, 60·7; H, 5·6; N, 15·7%)] in anhydrous ether (120 ml.) was slowly added under nitrogen to a stirred solution of methylmagnesium iodide prepared from magnesium (9·1 g.) and methyl iodide (53 g.) in ether (100 ml.). The mixture was boiled under reflux for 6 hr., kept at room temperature for 12 hr., then worked up as before, giving the pentanol (VI) in 72% yield.

*Oxidation of* 2 : 4-*Dimethyl*-4-*phenylpentan*-2-*ol* (VI).—A solution of chromium trioxide (42 g.) in water (70 ml.) and acetic acid (140 ml.) was added to 2 : 4-dimethyl-4-phenylpentan-2-ol (VI) (15·0 g.) (free from 4-methyl-4-phenylpentan-2-one) in acetic acid (70 ml.), and the mixture was stirred for 6 hr. at 60°, and poured into water (1 l.) and extracted with ether (4 × 450 ml.). The extracts were concentrated, shaken repeatedly with water to remove acetic acid, then twice with 10% aqueous sodium hydrogen carbonate (80 ml.), the solvent removed, and the residual oil (7·6 g.) steam-distilled. The distillate (100 ml.) yielded liquid fractions, b. p. 85—115°/18 mm. (0·91 g.) and b. p. 115—125°/18 mm. (0·78 g.); the first proved to be essentially acetophenone [2 : 4-dinitrophenylhydrazone from benzene–alcohol (Found: C, 55·2; H, 3·8; N, 18·7. Calc. for $C_{14}H_{12}O_4N_4$: C, 56·0; H, 4·0; N, 18·7%), m. p. and mixed m. p. 246°], and the second was characterised as 4-methyl-4-phenylpentan-2-one (VIII) (2 : 4-dinitrophenylhydrazone m. p. and mixed m. p. 97—97·5°). The residue from the steam-distillation yielded a further quantity (4·59 g.) of ketone (VIII) characterised as before [total yield of (VIII), 5·37 g.].

The above aqueous alkaline layer was acidified and extracted with ether. The extract yielded a product which was distilled; the main fraction (2·44 g.), b. p. 108—116°/0·4 mm., partially solidified, and after being sublimed twice at 70°/12 mm. and crystallised from dilute acetic acid, formed needles, m. p. 76·5—78° (Found: C, 73·2; H, 7·6. Calc. for $C_{10}H_{12}O_2$: C, 73·2; H, 7·3%); the mixed m. p. with α-methyl-α-phenylpropionic acid (IX) (m. p. 77—78°) was 77—78°.

α-*Methyl*-α-*phenylpropionic Acid* (IX).—Powdered aluminium bromide (64 g.) was added to a vigorously stirred solution of α-bromo-α-methylpropionic acid (10 g.) in anhydrous benzene (64 ml.), and the stirred mixture heated in an oil-bath at 150° for 2 hr. The cooled mixture was poured into dilute hydrochloric acid, the benzene layer and extract were shaken with water and with 10% aqueous potassium carbonate; acidification of the alkaline solution precipitated α-methyl-α-phenylpropionic acid (8·24 g., 82%), m. p. 77—78°.

This acid was previously prepared by Wallach [6a] by condensation of ethyl α-bromo-α-methylpropionate with benzene in presence of aluminium bromide; the original paper is not readily available, and the only two abstracts [6b,c] erroneously state that the reaction was carried out with the *acid*, which, however, under the conditions described by Wallach for the ester, gives a negligible yield of α-methyl-α-phenylpropionic acid.

*Oxidation of* tert.-*Butylbenzene*.—To *tert*.-butylbenzene [7] (14·6 g.) in acetic acid (70 ml.) was added chromium trioxide (90 g.) in acetic acid (300 ml.) and water (150 ml.), and the mixture was kept at 80° for 8 hr., then poured into water; the acidic material other than acetic acid was isolated as in the case of the similar oxidation of the alcohol (VI). This product (1·2 g.) proved to be trimethylacetic acid; it was converted into the acid chloride by means of thionyl chloride and thence into the anilide which, after crystallisation from ethanol, had m. p., and mixed m. p. with an authentic specimen, [8] 133°.

THE UNIVERSITY, BRISTOL. [*Received, November 12th*, 1957.]

[5] Hoffman, *J. Amer. Chem. Soc.*, 1929, **51**, 2543.
[6] (a) Wallach, *Nachr. K. Ges. Wiss. Göttingen*, 1899, 126; (b) *Chem. Soc. Abstracts*, 1900, **78**, 229; (c) *Chem. Zentr.*, 1899, II, 1047.
[7] Norris and Sturgis, *J. Amer. Chem. Soc.*, 1939, **61**, 1413.
[8] Degnan and Shoemaker, *ibid.*, 1946, **68**, 104.

## 202. *Parachors and Molecular Structure of Some Metal Alkoxides.*

By D. C. Bradley, (Miss) C. C. A. Prevedorou, J. D. Swanwick, and W. Wardlaw.

The densities and surface tensions of several alkoxides of titanium, zirconium, tin, cerium, and thorium have been measured over the temperature range 25—40° and the parachors have been calculated. Analysis of the parachors by the method used for alkyl orthogermanates [1] revealed some characteristic structural features. Parachor "contractions" in titanium *n*-alkoxides are consistent with the polymeric nature of these compounds and, in the monomeric tertiary alkoxides of titanium, zirconium, tin, cerium or thorium, suggest the presence of considerable intramolecular congestion accentuated by metal–oxygen bond contraction.

Recently [1] we reported the molar volumes and parachors of a representative range of alkyl orthogermanates and demonstrated the use of the parachor in the conformational analysis of molecules of that type. These monomeric germanium compounds were chosen as representative of the type $M(OR)_4$ containing the central atom M tetrahedrally bonded to oxygen because they were free from the complications of strong intermolecular bonding involving the metal and oxygen. We now report the results obtained with a number of liquid metal alkoxides with M = Ti, Zr, $Ce^{IV}$, $Sn^{IV}$, or Th over the temperature range 25—40°. Since the vapour pressures of these compounds are negligible in this region the parachor $[P]$ was calculated by using the simple equation $[P] = \gamma^{\frac{1}{4}}V$, where $\gamma$ is the surface tension and $V$ the molar volume. We have analysed these parachors by Gibling's method. This involves, first, subtraction of the expansion correction (E.C.) interpolated from Gibling's Table [2] to give the reduced parachor (R.P.). Next the sum of the reduced group parachors for the alkyl groups ($\sum$R.P. Alkyls) was calculated by using the following values: $CH_3(C) = 55{\cdot}2$; $(C)CH_2(C) = 39{\cdot}8$; $(C)CH_2(O) = 39{\cdot}3$; $(C)_2CH(C) = 22{\cdot}2$; $(C)_2CH(O) = 21{\cdot}2$: $(C)_2C(C)_2 = 2{\cdot}4$; and $(C)_3C(O) = 0{\cdot}9$. The reduced parachor for the pentatomic group of metal and four oxygen atoms was then obtained from the equation, R.P. $M(O_4)$ = R.P. − $\sum$R.P. Alkyls. In this procedure no assumptions are made concerning parachor values either for the metal or for oxygen attached to metal. It is clear that in the absence of

Table 1.

| | $M(OR)_4$ | $[P]$ | E.C. | R.P. | $\sum$R.P. Alkyls | R.P.$M(O_4)$ |
|---|---|---|---|---|---|---|
| M | R | | | | | |
| Ti | Et | 454 | 2·0 | 452 | 378·0 | 74 |
| ,, | $Pr^n$ | 616 | 3·7 | 612 | 537·2 | 75 |
| ,, | $Bu^n$ | 769 | 5·8 | 763 | 696·4 | 67 |
| ,, | $Bu^t$ | 844·5 | 7·0 | 837 | 666·0 | 171 |
| ,, | $CMe_2Et$ | 989 | 9·8 | 979 | 825·2 | 154 |
| ,, | $CMe_2Pr^n$ | 1154·5 | 13·3 | 1141 | 984·4 | 157 |
| ,, | $CMeEt_2$ | 1120·5 | 12·5 | 1108 | 984·4 | 124 |
| Zr | $Bu^t$ | 851·5 | 7·0 | 844 | 666·0 | 178 |
| ,, | $CMe_2Et$ | 992 | 9·8 | 982 | 825·2 | 157 |
| ,, | $CMe_2Pr^n$ | 1154·5 | 13·3 | 1141 | 984·4 | 157 |
| ,, | $CMeEt_2$ | 1121 | 12·5 | 1109 | 984·4 | 125 |
| $Sn^{IV}$ | $CMe_2Et$ | 919·5 | 8·4 | 911 | 825·2 | 86 |
| ,, | $CMe_2Pr^n$ | 1088 | 11·8 | 1076 | 984·4 | 92 |
| $Ce^{IV}$ | $CMeEt_2$ | 1130·5 | 12·7 | 1118 | 984·4 | 134 |
| ,, | $CEt_2$ | 1269 | 16·1 | 1253 | 1143·6 | 109 |
| Th | $CEt_2$ | 1231·5 | 15·2 | 1216 | 1143·6 | 72 |

volume anomalies the value of R.P.$MO_4$ should be constant for a given metal irrespective of the alkyl group. The results are given in Table 1 in which $[P]$ is the average parachor over the temperature range studied.

[1] Bradley, Kay, and Wardlaw, *J.*, 1956, 4916.
[2] Gibling, *J.*, 1941, 299.

We consider first the values of the reduced parachor for the group $Ti(O)_4$. The most striking feature is the enormous difference between values for the *n*-alkoxides and *tert.*-alkoxides. This is undoubtedly a consequence of the polymeric nature of the *n*-alkoxides compared with the monomeric *tert.*-alkoxides. For example, it has been shown that titanium tetraethoxide approaches a limiting trimeric state in either benzene [3] or ethanolic [4] solutions and it is probable that the liquid ethoxide consists mainly of trimeric molecules. Further, it has been suggested [3,4] that the trimeric ethoxide contains titanium 6-co-ordinated by oxygen in approximately octahedral configuration and it is evident that the formation of such a trimer leads to a considerable loss of volume relative to that of the monomer. The value of $R.P.Ti(O)_4$ is not constant for the *n*-alkoxides but is in the order: *n*-propyl > ethyl > *n*-butyl. The appearance of a maximum value of $R.P.Ti(O)_4$ in the *n*-propoxide is consistent with the operation of two structural phenomena in the titanium *n*-alkoxides, as was previously suggested to explain trends in the entropies of vaporisation.[6] Thus it has been shown by molecular-weight determinations that the degree of polymerisation in titanium *n*-alkoxides decreases with increase in length of alkyl chain [3,5,6] and this should cause a variation in $R.P.Ti(O)_4$ in the order: *n*-butyl > *n*-propyl > ethyl. On the other hand it was suggested [6] that in ascending the homologous series another type of interaction involving the *n*-alkyl chains becomes increasingly important. This alkyl interaction which we visualised as an intermolecular " entanglement " of the alkyl chains will cause a volume loss leading to a variation in $R.P.Ti(O)_4$ in the order: ethyl > *n*-propyl > *n*-butyl, and it is the simultaneous operation of these two opposed structural effects which results in the *n*-propoxide's having the maximum value of $R.P.Ti(O)_4$ and the minimum entropy of vaporisation.

A second notable feature of the results on titanium alkoxides is the pronounced decrease in $R.P.Ti(O)_4$ with the increased branching of the alkyl group in the *tert.*-alkoxides. This effect is also clearly apparent in the values of $R.P.Zr(O)_4$ for zirconium *tert.*-alkoxides and in $R.P.Ce^{IV}(O)_4$ for the two cerium compounds. Moreover a similar effect of chain branching was observed in the alkyl orthogermanates [1] and it is evidently a consequence of a fundamental structural feature of this type of molecule. Previously [1] we showed that this effect was caused by intramolecular congestion which by virtue of the overlap of van der Waals volumes of some of the atoms led to an effective loss of volume. This was confirmed by measurements on molecular models which showed qualitative agreement between volume losses calculated for conformations of minimum intramolecular congestion and the observed parachor losses. Similarly, in the series $M(O{\cdot}CMe_xEt_{3-x})_4$ where M = Ti or Zr and $x = 3$, 2, or 1, the value of $R.P.M(O)_4$ decreases sharply as $x$ decreases. It is particularly noteworthy that the derivatives of 2-methylpentan-2-ol have values of $R.P.M(O)_4$ greater than those of the derivatives of the isomeric 3-methylpentan-3-ol. In fact the derivatives of the former alcohol gave values equal to, or slightly higher than, those of *tert.*-amyl alcohol. This behaviour agrees with the predictions of conformational analysis, it being assumed that the molecules are predominantly in the conformations of minimum intramolecular congestion (see ref. 1 for illustrations of these conformations for *tert.*-butyl and *tert.*-amyl orthogermanates). Thus in converting the *tert.*-amyloxide into the derivative of 2-methylpentan-2-ol the molecule is extended at peripheral positions and no additional volume loss is involved, whereas in the formation of the derivative of 3-methylpentan-3-ol there is more intramolecular congestion.

A third notable feature of Table 1 is revealed in a comparison of values of $R.P.M(O)_4$ in a series of alkoxides containing the same alkyl group but different metals. In terms of purely stereochemical factors it would be predicted that volume losses due to intramolecular congestion in the tertiary alkoxides should decrease with increase in size of

[3] Caughlan, Smith, Katz, Hodgson, and Crowe, *J. Amer. Chem. Soc.*, 1951, **73**, 5652.
[4] Bradley, Gaze, and Wardlaw, *J.*, 1955, 3977.
[5] Cullinane, Chard, Price, Millward, and Langlois, *J. Appl. Chem.*, 1951, **1**, 400.
[6] Bradley, Mehrotra, Swanwick, and Wardlaw, *J.*, 1953, 2025.

XUM

the central atom and that for a given alkyl group the value of $R.P.M(O)_4$ should depend on the atomic radius of M. Hence we should expect the R.P. order: $Th(O)_4 > Ce^{IV}(O)_4 > Zr(O)_4 > Sn^{IV}(O)_4 > Ti(O)_4$. This is clearly not the case because our results show $Ti(O)_4 \gg Sn^{IV}(O)_4$, and $Ce^{IV}(O)_4 > Th(O)_4$, while $Ti(O)_4$ is almost as large as $Zr(O)_4$. In view of the results on titanium *n*-alkoxides which showed the striking effect of polymerisation it could be argued that, contrary to the apparent monomeric nature of the *tert.*-alkoxides in solution, they might not be exactly monomeric in the liquid state and that a small degree of polymerisation would explain these anomalies. However there are two reasons for rejecting such an argument. First, the degree of polymerisation for a given metal would decrease with increase in branching of the alkyl group and this would cause an increase in $R.P.M(O)_4$ instead of the observed decrease. Secondly, the monomeric nature of several of these *tert.*-alkoxides is confirmed by data on vapour pressures and entropies of vaporisation. It appears that electronic factors must also be considered and it seems reasonable to suggest that the M–O bonds are thus shortened so that the covalent atomic radii are not applicable. In particular it is considered that intramolecular covalency expansion occurs in the form of double bonding $^{-}M{=}O^{+}R$ and that this is stabilised by electron release from the *tert.*-alkyl group. The extent of partial double bonding will vary according to the metal involved, but at present there is a dearth of reliable data on interatomic distances for these molecules and it would be unwise to speculate further on this aspect. It is of interest to apply Gibling's method to the problem of the " anomalies " found by Mann and Purdie [7] in the parachors of some complexes of palladous chloride. We offer the following interpretation of Mann and Purdie's results. We have treated their data in the same manner as for the metal alkoxides, using the same values for reduced group parachors. In the case of *trans*-bis(dialkyl sulphide) palladous chlorides the reduced group parachor for the pentatomic system $[S_2PdCl_2]$ was calculated by using $(C)CH_2(S) = 39{\cdot}3$ and $CH_3(S) = 54{\cdot}7$. For the trialkylphosphine complexes the reduced group parachor for $[\{(CH_2)_3P\}_2PdCl_2]$ was deduced because the value for $(C)CH_2(P)$ has not been determined. Similarly for the trialkylarsine complexes the value for $[\{(CH_2)_3As\}_2PdCl_2]$ was calculated. These results are given in Table 2.

TABLE 2.

| | *trans*-$(R_2S)_2PdCl_2$ | | | *trans*-$(R_2P)_2PdCl_2$ | | | *trans*-$(R_2As)_2PdCl_2$ | | |
|---|---|---|---|---|---|---|---|---|---|
| R | [*P*] | $[S_2PdCl_2]$ | Δ | [*P*] | $[\{(CH_2)_3P\}_2PdCl_2]$ | Δ′ | [*P*] | $[\{(CH_2)_3As\}PdCl_2]$ | Δ′ |
| Me ..... | 463 | 242 | 0 | — | — | — | — | — | — |
| Et ..... | 613 | 231 | −11 | 775 | 438 | 0 | 793 | 456 | 0 |
| Pr$^n$ ..... | 760 | 217 | −25 | 994 | 414 | −24 | 1014 | 434 | −22 |
| Bu$^n$ ..... | 906 | 198 | −44 | 1217 | 393 | −45 | 1243 | 419 | −37 |
| Bu$^i$ ..... | 914 | 218 | −24 | — | — | — | — | — | — |
| *n*-$C_5H_{11}$ ... | 1054 | 187 | −55 | 1452 | 383 | −55 | 1467 | 398 | −58 |

These results show clearly for each type of compound that there is a parachor contraction between each homologue in ascending the *n*-alkyl series. This is shown by the increments Δ or Δ′. We are convinced that this is a genuine structural phenomenon caused by the alignment of the *n*-alkyl chains and that it is not due to the fact that the central atom is a metal. The same behaviour is shown by *n*-alkyl orthocarbonates and orthosilicates (Arbusov and Vinogradova [8]); and for dialkyl carbonates, malonates, sulphates, and sulphites, and for trialkyl phosphates and phosphites Gibling [9] has observed similar effects in the *n*-alkyl derivatives. It appears that *n*-alkyl chains radiating from a central atom or group tend to align themselves in parallel so that they sweep out a smaller van der Waals volume than in the pure hydrocarbon. We discussed this in terms of models for the *n*-alkyl germanates [1] and showed that reasonable agreement was obtained between observed and calculated molar volumes. Returning to Mann and Purdie's compounds we

[7] Mann and Purdie, *J.*, 1935, 1549.
[8] Arbusov and Vinogradova, *Doklady Akad. Nauk S.S.S.R.*, 1948, **60**, 799.
[9] Gibling, *J.*, 1941, 304; 1944, 383.

find strong support for our views in the behaviour of *trans*-bis(di*iso*butyl sulphide) palladous chloride which has a much smaller Δ than the *n*-butyl isomer. This is because the *iso*-butyl groups can only align themselves to the same degree as *n*-propyl groups, a view confirmed by the Δ value for the *n*-propyl derivative which is practically the same as for the *iso*butyl derivative. Mann and Purdie [7] also determined parachors for a number of *n*-alkylthiomercury compounds and we have deduced the corresponding values of $[S_2Hg]$ (Table 3). Again there is a contraction between each homologue, and the increment Δ

TABLE 3.

| R in $Hg(SR)_2$ | $[P]$ | $[S_2Hg]$ | Δ | Δ′ | R | $[P]$ | $[S_2Hg]$ | Δ | Δ′ |
|---|---|---|---|---|---|---|---|---|---|
| Et | 334 | 144 | 0 | 0 | $n$-$C_6H_{13}$ | 620 | 109 | −35 | −5 |
| $Pr^n$ | 402 | 131 | −13 | −13 | $n$-$C_7H_{15}$ | 692 | 100 | −44 | −9 |
| $Bu^n$ | 475 | 125 | −19 | − 6 | $n$-$C_8H_{17}$ | 772 | 99 | −45 | −1 |
| $n$-$C_5H_{11}$ | 545 | 114 | −30 | −11 | | | | | |

becomes more negative in ascending the series. However, the increment Δ′ between succeeding members shows an alternating magnitude reminiscent of the alternation found in the *n*-alkyl orthosilicates (see ref. 1). Unfortunately Mann and Purdie did not study this series with branched alkyl groups but we would predict that branching would lead to higher values of $[S_2Hg]$ than for the *n*-alkyl isomers.

## EXPERIMENTAL

*Preparation of Metal Alkoxides.*—The alkoxides of titanium,[6,10] zirconium,[6,10] tin,[11] cerium,[12] and thorium [13] were prepared, purified, and analysed by the methods already described.

*Density and Surface-tension Measurements.*—An all-glass dilatometer of *ca.* 11 c.c. capacity fitted with two limbs of "Veridia" capillary tubing was used. It differed from that described in the germanium work [1] by having only one standard joint. Since the capillaries ($r_1$ = 0·0245 cm., $r_2$ = 0·1246 cm.) differed markedly in bore it was possible to calculate the density and surface tension of the liquid from the same measurement. The cleaning, drying, and weighing technique was similar to that described earlier.[1] The alkoxide was collected in the dilatometer by fractional distillation under 0·05 mm. pressure, in an all-glass apparatus fitted with a variable take-off still-head and a device for taking fractions without interrupting the distillation. At least three separate determinations were carried out over the whole temperature range on each

TABLE 4.

| Compound | $d_0$ | α | $\gamma_0$ | β |
|---|---|---|---|---|
| $Ti(OEt)_4$ | 1·1321 | 0·00102 | 23·77 | 0·027 |
| $Ti(OPr^n)_4$ | 1·0564 | 0·00086 | 27·38 | 0·079 |
| $Ti(OBu^n)_4$ | 1·0160 | 0·00081 | 27·00 | 0·060 |
| $Ti(OBu^t)_4$ | 0·9060 | 0·00090 | 24·38 | 0·059 |
| $Ti(O\text{-}CMe_2Et)_4$ | 0·9239 | 0·00076 | 27·33 | 0·061 |
| $Ti(O\text{-}CMe_2Pr^n)_4$ | 0·9085 | 0·00075 | 27·15 | 0·038 |
| $Ti(O\text{-}CMeEt_2)_4$ | 0·9437 | 0·00069 | 29·22 | 0·065 |
| $Zr(OBu^t)_4$ | 0·9845 | 0·00110 | 22·34 | 0·080 |
| $Zr(O\text{-}CMe_2Et)_4$ | 0·9960 | 0·00093 | 24·11 | 0·050 |
| $Zr(O\text{-}CMe_2Pr^n)_4$ | 0·9719 | 0·00082 | 25·40 | 0·060 |
| $Zr(O\text{-}CMeEt_2)_4$ | 1·0092 | 0·00081 | 25·79 | 0·042 |
| $Sn(O\text{-}CMe_2Et)_4$ | 1·1229 | 0·00098 | 23·26 | 0·061 |
| $Sn(O\text{-}CMe_2Pr^n)_4$ | 1·0724 | 0·00090 | 23·52 | 0·042 |
| $Ce(O\text{-}CMeEt_2)_4$ | 1·1064 | 0·00114 | 24·55 | 0·011 |
| $Ce(O\text{-}CEt_3)_4$ | 1·0879 | 0·00078 | 25·83 | 0·014 |
| $Th(O\text{-}CEt_3)_4$ | 1·2505 | 0·00110 | 22·61 | 0·027 |

alkoxide. The results are presented in Table 4 in the abbreviated form, involving the appropriate constants $d_0$, α, $\gamma_0$, and β, where $d_t$ (density at $t°$) = $d_0 - \alpha t$, and $\gamma$ (surface tension at $t°$) = $\gamma_0 - \beta t$.

[10] Bradley, Mehrotra, and Wardlaw, *J.*, 1952, 4204.
[11] Bradley, Caldwell, and Wardlaw, *J.*, 1957, 4775.
[12] Bradley, Chatterjee, and Wardlaw, *J.*, 1957, 2600.
[13] Bradley, Saad, and Wardlaw, *J.*, 1954, 3488.



XUM

*Parachors.*—The values for the parachor at various temperatures are given in Table 5. It is difficult to estimate the probable error in these measurements. Although separate experiments on the same compound gave results which agreed within ~0·2% it is possible, in view of the ease of hydrolysis of these compounds, that the absolute error could be 0·5—1·0%. Apart from titanium *n*-propoxide and zirconium *tert.*-butoxide which gave remarkably constant values, there is a small but general drift towards higher values of the parachor at higher temperatures and this is most marked for the two cerium compounds. For all of the other compounds the variation of parachor with temperature (~0·03% per degree) is much smaller than the variation

TABLE 5. *Parachors* [*P*].

| Compound | 25° | 30° | 35° | 40° |
|---|---|---|---|---|
| $Ti(OEt)_4$ | 452·1 | 453·6 | 454·6 | 456·3 |
| $Ti(OPr^n)_4$ | 616·4 | 616·5 | 616·4 | 616·4 |
| $Ti(OBu^n)_4$ | 767·7 | 768·3 | 769·1 | 770·0 |
| $Ti(OBu^t)_4$ | 842·0 | 844·0 | 845·3 | 846·7 |
| $Ti(O{\cdot}CMe_2Et)_4$ | 987·5 | 988·6 | 990·0 | 991·0 |
| $Ti(O{\cdot}CMe_2Pr^n)_4$ | 1150·5 | 1153·5 | 1155·7 | 1158·7 |
| $Ti(O{\cdot}CMeEt_2)_4$ | 1119·5 | 1120·2 | 1121·2 | 1121·5 |
| $Zr(OBu^t)_4$ | 851·0 | 851·5 | 852·1 | 851·3 |
| $Zr(O{\cdot}CMe_2Et)_4$ | 988·8 | 990·7 | 993·2 | 994·4 |
| $Zr(O{\cdot}CMe_2Pr^n)_4$ | 1152·5 | 1153·8 | 1155·0 | 1156·8 |
| $Zr(O{\cdot}CMeEt_2)_4$ | 1118·0 | 1120·2 | 1122·2 | 1125·0 |
| $Sn(O{\cdot}CMe_2Et)_4$ | 918·2 | 919·2 | 920·0 | 920·9 |
| $Sn(O{\cdot}CMe_2Pr^n)_4$ | 1085·2 | 1087·8 | 1088·5 | 1091·0 |
| $Ce(O{\cdot}CMeEt_2)_4$ | 1122·5 | 1127·5 | 1133·3 | 1138·5 |
| $Ce(O{\cdot}CEt_3)_4$ | 1263·8 | 1267·3 | 1270·7 | 1275·5 |
| $Th(O{\cdot}CEt_3)_4$ | 1226·8 | 1230·0 | 1234·0 | 1235·2 |

of molar volume with temperature (~0·1% per degree) and it seems reasonable to choose the average parachor for comparative purposes.

BIRKBECK COLLEGE, MALET STREET, LONDON, W.C.1. [*Received, December 20th*, 1956.]

---

## 203. *Properties of Ion Pairs formed by Proton Transfer to Methoxyphenylpolyenealdehydes.*

By A. WASSERMANN.

The light-absorption spectra of ω-*p*-methoxyphenylpolyenealdehydes with 1—7 conjugated double bonds have been measured with and without trichloroacetic acid in benzene and in benzene–dioxan. The observed effects, together with the results of electrical conductivity measurements, show that proton transfer from the acid to the polyenes takes place. Equilibrium coefficients of these reactions have been determined.

THE basicity of carotene and azulene is sufficient for proton-transfer reactions to be studied in aprotic solvents. It is of interest to extend earlier experiments [1,2] by varying the nature of the conjugated polyene, in a systematic manner, while using one and the same acid. The present investigation deals with the proton-acceptor properties of ω-*p*-methoxyphenylpolyenealdehydes,[3] $MeO{\cdot}C_6H_4{\cdot}[CH{:}CH]_n{\cdot}CHO$ ($n = 1$—7), the proton donor being trichloroacetic acid.

### EXPERIMENTAL

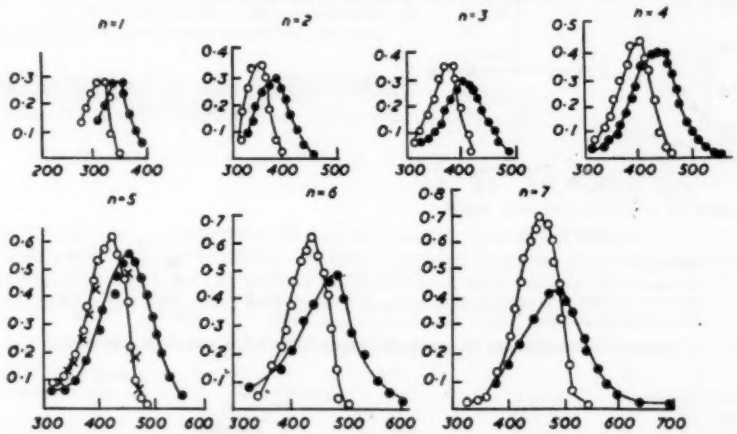
The seven polyenealdehydes were kept in evacuated containers at 0° in the dark until shortly before use. The m. p.s agreed with the published values.[3] Commercial dioxan was dried and redistilled. The purification of trichloroacetic acid, ethyl trichloroacetate, and benzene, and the techniques used for carrying out spectrophotometric and conductivity measurements have

[1] Wassermann, *J.*, 1954, 4239.
[2] Wassermann, *ibid.*, 1955, 585.
[3] Marshall and Whiting, *ibid.*, 1956, 4082.

been described.[1] In the optical tests, the solutions contained the antioxidant α-tocopherol in concentration about 20 times smaller than that of the polyene. Control experiments showed that α-tocopherol had no effect, except to prevent a small drift of the optical densities of solutions containing acid. Concentrations of trichloroacetic acid were calculated from the stoicheiometric molecular weight, as in previous papers; [1,2,4] it is realised that this acid forms a dimer under the conditions of these experiments.

*Results.*—The light absorption of these polyenealdehydes with and without trichloroacetic acid in benzene solution is shown in Fig. 1. On addition of acid there is a shift of the spectra

FIG. 1. *Light absorption of ω-p-methoxyphenylpolyenealdehydes.*




$n$ = no. of conjugated double bonds. Temp. ~20°. Ordinate, $10^{-5}\varepsilon$; abscissa, wavelength (mμ). Solvents: ○, benzene (no acid); ×, benzene, 1·0M with respect to ethyl trichloroacetate; ●, benzene. 1·84M with respect to trichloroacetic acid.

towards longer wavelength, which is responsible, in most cases, for a visual change of colour (Table 1). The spectra of these polyenes were also measured in a benzene solution which was

TABLE 1. *Colour of benzene solutions of ω-p-methoxyphenylpolyenealdehydes.* (In these tests the solution was ~$10^{-5}$M in polyene and ~0·5M in trichloroacetic acid; temp. ~20°.)

| No. of conjugated double bonds, $n$ ... | 1 | 2 | 3 | 4 | 5, 6, 7 |
|---|---|---|---|---|---|
| Without acid ..... | Colourless | Colourless | Pale yellow | Pale yellow | Yellow |
| With acid ..... | Colourless | Pale yellow | Yellow | Deep yellow | Red |

1M with respect to ethyl trichloroacetate, in benzene–dioxan, and in chloroform. The absorption spectra are not significantly altered by addition of dioxan and ethyl trichloroacetate, or by using chloroform instead of benzene. This is shown in Figs. 1 and 5 and in Table 2, where $\lambda_{max.}$ and $\varepsilon_{max.}$ in the range 290—1000 mμ are listed. (For definition of ε see ref. 1; the values for chloroform solution were taken from ref. 3.)

The relatively large alteration of the spectra on addition of acid (A) is interpreted as being due to a proton transfer from (A) to the polyene (B):

$$\alpha A + B \rightleftharpoons C^+ \ldots . D^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $C^+ \ldots . D^-$ is an ion pair. The proportion of B converted into $C^+ \ldots . D^-$ can be determined by measuring optical density as a function of acid concentration, as shown in Fig. 2 for the polyenes with $n$ = 1, 4, and 7. Similar results were obtained with light of other wavelengths, with solutions of the other polyenes, and with different concentrations of these proton

[4] Rubin, Steiner, and Wassermann, *J.*, 1949, 3046.

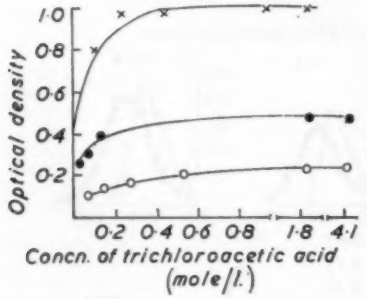
XUM

acceptors. It is assumed, as before,[1,2] that $\alpha$ in eqn. (1) is unity and that the equilibrium coefficient of this proton transfer is given by

$$K = ([C^+ \ldots . D^-]/[A][B]) \times f_{C^+ \ldots . D^-}/f_A \times f_B$$

where the factor in the round brackets, designated by $K'$, is estimated from optical densities, $K$ being deduced from $K'$ by an extrapolation method.[1,2] The assumption that $\alpha$ is unity is

FIG. 2. *Influence of trichloroacetic acid concentration on optical density.*

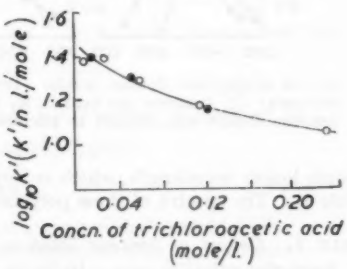



Solvent, benzene; temp., 20—21°; optical path length, 1·00 cm.

| | | | |
|---|---|---|---|
| Symbol | × | ● | ○ |
| $n$ | 1 | 4 | 7 |
| Polyene concn. (mole/l. × $10^5$) | 5·52 | 1·52 | 1·14 |
| Wavelength of light (mμ) | 360 | 460 | 560 |

The part of the abscissa covering the range 0·9—4·1 is not drawn to scale.

FIG. 3. *Equilibrium measurements with polyene, $n = 3$. Influence of the trichloroacetic acid concentration on* $\log_{10} K'$.




Solvent, benzene; temp., 21°; wavelength, 440 mμ; $10^5$[polyene]: ○ = 1·64, ● = 4·92. Value of $(\log_{10} K')_{[A]\to 0} = 1·47 \pm 0·02$; $K = 30 \pm 3$ l./mole.

TABLE 2. *Light absorption* ($\lambda$ *in* mμ) *of* ω-p-*methoxyphenylpolyenealdehydes.*

(Solvents: b = benzene; b + d = benzene, 4·54M in dioxan; c = chloroform. Temp. ~20°.)

| | | Without acid | | 1·84M-$CCl_3$·$CO_2H$ | | | | Without acid | | 1·84M-$CCl_3$·$CO_2H$ | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $n$ | Solvent | $\lambda_{max.}$ | $10^{-5}\varepsilon_{max.}$ | $\lambda_{max.}$ | $10^{-5}\varepsilon_{max.}$ | $n$ | Solvent | $\lambda_{max.}$ | $10^{-5}\varepsilon_{max.}$ | $\lambda_{max.}$ | $10^{-5}\varepsilon_{max}$ |
| 1 | b | 320 | 0·28 | 345 | 0·28 | 5 | b | 420 | 0·62 | 450 | 0·57 |
| | b + d | 320 | 0·27 | | | | b + d | 420 | 0·65 | | |
| | c | 321 | 0·31 | | | | c | 426 | 0·68 | | |
| 2 | b | 350 | 0·35 | 380 | 0·30 | 6 | b | 440 | 0·63 | 475 | 0·48 |
| | b + d | 350 | 0·33 | | | | b + d | 440 | 0·62 | | |
| | c | 352 | 0·42 | | | | c | 443 | 0·77 | | |
| 3 | b | 375 | 0·34 | 410 | 0·29 | 7 | b | 455 | 0·68 | 485 | 0·43 |
| | b + d | 378 | 0·38 | | | | b + d | 460 | 0·53 | | |
| | c | 380 | 0·52 | | | | c | 459 | 0·90 | | |
| 4 | b | 400 | 0·42 | 435 | 0·38 | | | | | | |
| | b + d | 400 | 0·42 | | | | | | | | |
| | c | 403 | 0·61 | | | | | | | | |

consistent with the observation that $(K')_{[A]\to 0}$ is independent of the initial concentration of the polyene, [B], within the limits of the specified experimental error. If it is assumed that $\alpha > 1$ or $\frac{1}{2}$ the extrapolated $K'$ values depend on [B]. For the polyene with $n = 3$, for example, measurements at different acid concentrations with [B] = $1·65 \times 10^{-5}$ and

$4{\cdot}92 \times 10^{-5}$ mole/l. were carried out. In both sets $K'_{[A]\to 0}$ was $30 \pm 3$ l./mole, if $\alpha$ was taken as unity. If, however, an $\alpha$ value of 2 was employed, extrapolated $K'$ values of respectively $4 \times 10^3$ and $8 \times 10^3$ (l./mole)$^2$ were computed; and similar discrepancies occur if it is assumed that $\alpha = \frac{1}{2}$. An alternative expression of a " concentration " equilibrium coefficient, in which activity corrections are omitted, is [5] $K'' = S/i$, where $S$ is the slope and $i$ the intercept of the plot of $[A][B]/d_A$ against [A] ($d_A$ = optical density). $K''$ can be determined, with sufficient

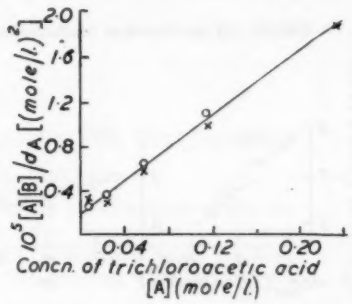



FIG. 4. *Equilibrium measurements with polyene, $n = 4$. Influence of trichloroacetic acid concentration on* $[A][B]/d_A$ *(for significance of symbols, see text).*

Solvent, benzene; temp., 20°: wavelength 480 mμ; optical path length, 1·00 cm.; $10^5$[Polyene]: × = 1·52; ○ = 4·56; $K''$ = slope/intercept = $33 \pm 3$ l./mole.

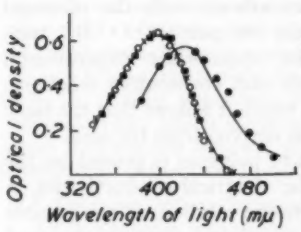
accuracy, by varying [A] between 0·02 and 0·2 mole/l., whereas an estimation of $K'$ involves measurements with [A] > 0·5 mole/l. Results of typical experiments showing the dependence of log $K'$ and of $[A][B]/d_A$ on [A] are in Figs. 3 and 4. Table 3 shows the values of $K$ and $K''$, the wavelengths of the light used, and the polyene concentrations.

TABLE 3. *Equilibrium coefficients of proton-transfer reactions in benzene at ~20°.*

| No. of conjugated double bonds, $n$ | $K$ (l./mole) | $K''$ (l./mole) | λ (mμ) | $10^5$[polyene] |
|---|---|---|---|---|
| 1 | $25 \pm 3$ | $28 \pm 3$ | 350, 360 | 1·84, 5·52 |
| 2 | $30 \pm 4$ | $25 \pm 3$ | 400 | 3·12 |
| 3 | $30 \pm 3$ | $30 \pm 4$ | 420, 440, 460 | 1·64, 4·92 |
| 4 | $32 \pm 3$ | $33 \pm 4$ | 460 | 1·52, 4·56 |
| 5 | $32 \pm 3$ | $31 \pm 3$ | 480, 500 | 1·33, 3·99 |
| 6 | $36 \pm 4$ | $34 \pm 4$ | 520 | 1·12, 3·36 |
| 7 | $32 \pm 3$ | $31 \pm 3$ | 560 | 0·114, 1·14 |

If benzene solutions of these polyenes, B, are made 4—5M with respect to dioxan no significant change occurs in the spectra. If, on the other hand, the same amount of dioxan is added to a benzene solution of the polyene–trichloroacetic acid adduct, $C^+ \ldots D^-$, there is a change of the spectra as shown by the typical results in Fig. 5. Similar observations were made with all the other polyenes.

FIG. 5. *Influence of dioxan on the light absorption by an adduct* $C^+ \ldots D^-$; *experiments with polyene, $n = 4$.*




Solvent, benzene; temp., 21°; optical path length, 1·00 cm.
A solution was made, $3 \times 10^{-5}$M in polyene and 0·2M in trichloroacetic acid; immediately after mixing, solvent and dioxan were added, the final solution being 4·54M in dioxan, $1{\cdot}52 \times 10^{-5}$M in polyene, and 0·115M in acid. Results with this solution are denoted by ×; those with other solutions were:

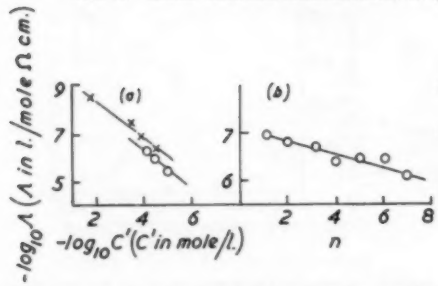
$1{\cdot}52 \times 10^{-5}$M in polyene and 0·115M in acid; no dioxan ..... ●
$1{\cdot}52 \times 10^{-5}$M in polyene, 4·54M in dioxan; no acid ..... ○
$1{\cdot}52 \times 10^{-5}$M in polyene; no dioxan, no acid ..... ■

The specific electrical conductance, $\kappa$, of the adducts $C^+ \ldots D^-$ in benzene solution, 1·00M in trichloroacetic acid, is larger than that of the acid or the polyenes alone, as shown by the following typical figures, relating to 25·0° and to the polyene, $n = 1 : \kappa \times 10^{11}$ ($\Omega^{-1}$ cm.$^{-1}$) was $2{\cdot}48 \pm 0{\cdot}03$, $1{\cdot}00 \pm 0{\cdot}10$, and $0{\cdot}03 \pm 0{\cdot}01$, respectively, for solutions (i) $2{\cdot}76 \times 10^{-5}$M in

[5] Page, *Trans. Faraday Soc.*, 1953, **49**, 637.

polyene and 1·00M in acid, (ii) 1·00M in acid (no polyene), and (iii) $1{\cdot}84 \times 10^{-2}$M in polyene (no acid). Molar electrical conductivities, $\Lambda$, were computed from $\Lambda = (\kappa - \kappa')/c'$, where $\kappa$ and $\kappa'$ are the specific conductances of $C^+ \ldots . D^-$ in the presence of acid and of the acid alone and $C'$ is the concentration of $C^+ \ldots . D^-$, which is practically identical with the stoicheiometric concentration of B. The concentration dependence of $\Lambda$ as observed in two typical experiments, and the various $\Lambda$ values for a specified concentration $C'$, are in Fig. 6. The range of $C'$ values for the two polyenes with $n = 1$ and 7 is shown in Fig. 6(*a*). These

FIG. 6. *Molar electrical conductivities, Λ, of polyene aldehyde–trichloroacetic acid adducts.*




Solvent: benzene, 1·00M in trichloroacetic acid; temp. 25·0°.

(*a*) Typical concentration dependence: $C'$ is concentration of species $C^+ \ldots . D^-$ (see text). Polyene, $n = 7 \ldots \bigcirc$, polyene, $n = 1 \ldots \times$.

(*b*) Influence of number of conjugated double bonds, $n$, on $-\log_{10}\Lambda$; $C'$ in all tests = $1{\cdot}00 \times 10^{-4}$M.

polyenes are the most and the least soluble member of the series respectively;[3] the concentration range in the experiments with the other polyenes was intermediate between those specified in the Figure.

## DISCUSSION

The equilibrium coefficients are represented by $RT \ln K = T\Delta S - \Delta H = T\Delta S_g + T\Delta S_l - \Delta H_g - \Delta H_l$, where the overall entropy and heat changes, $\Delta S$ and $\Delta H$, are split into $\Delta S_g$ and $\Delta H_g$ relating to reaction (1) in the gas phase, and into $\Delta S_l$ and $\Delta H_l$, the entropies and heats of solution. Addition of protons to these methoxypolyenealdehydes leads to mesomeric carbonium-ion derivatives, which are stabilised by resonance energy. If it is assumed that the proton adds to the carbonyl or methoxy-groups, the resonance energy must increase with increasing number, $n$, of repeating CH:CH units; and it is probable, therefore, that the numerical value of $\Delta H_g$ will also increase on passing from the ion pair $(C^+ \ldots . D^-)_{n-1}$ to $(C^+ \ldots . D^-)_{n-7}$. The figures in Table 3 show, however, that the $K$ values relating to these proton additions in benzene solution remain practically constant. This is probably due to the fact that the trends of $\Delta H_g$ and $\Delta H_l$ oppose each other, the ion pair with the smallest number of conjugated double bonds being most extensively solvated, because of reduced delocalisation of the positive charge. Furthermore, the possibility must be considered of a second compensating mechanism, in which the influence of $\Delta H_g$ and $\Delta H_l$ is counteracted by that of $\Delta S_g$ and $\Delta S_l$.

The postulated proton transfer in reaction (1) is in accordance with the observed influence of the basic solvent dioxan, which decomposes the ion pair $C^+ \cdots D^-$, with quantitative re-formation of the polyenes. Thus, under appropriate experimental conditions, reaction (1) is not necessarily disturbed by side and consecutive reactions. These effects are shown by the typical results in Fig. 5, from which it follows that the basic solvent competes successfully with the polyene for the proton derived from the acid.

The charge separation in these proton-transfer reactions to polyenes is proved by the electrical conductance of the adducts $C^+ \ldots D^-$. The molar electrical conductivities, $\Lambda$ (Fig. 6), are either larger than those of authentic salts in benzene solution, at comparable concentration, or of the same order. Conductance maxima or minima were not observed in the limited range of concentration tested, there being a linear functional relation between log $\Lambda$ and the logarithm of the concentration, as in the previously investigated systems.[1,2] This indicates [6] that triple ions or higher aggregates play no significant rôle

[6] Fuoss and Krauss, *J. Amer. Chem. Soc.*, 1933, **55**, 2387; Hughes, Ingold, Patai, and Pocker, *J.*, 1957, 1206.

and that the carriers of electric current are formed by $C^+ \ldots D^- \rightleftharpoons C^+ + D^-$. This equilibrium must be far to the left-hand side, because the dielectric constant of solvent and co-solvent [7] is small.

A gift of the seven polyenealdehydes by Drs. D. Marshall and M. C. Whiting, and discussions with Professor D. Craig, Dr. A. Maccoll, and Dr. M. C. Whiting are gratefully acknowledged.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON. [*Received, July 10th*, 1957.]

[7] Le Fèvre and Vine, *J.*, 1938, 1795.

---

## 204. *Heats of Combustion. Part II.* The Six Lutidines.*

By J. D. COX and H. A. GUNDRY.

The heats of combustion, and hence the heats of formation, of the six isomeric lutidines (dimethylpyridines) have been determined by means of an electrically-calibrated bomb calorimeter. From the results, the heat change for the isomerisation of one liquid lutidine into another can be calculated.

HEATS of combustion of the six lutidines were measured. Although the heats of combustion of 2 : 5- and 2 : 6-lutidine were determined a few years ago,[1] it was decided to make further measurements on them because of the desirability of having values for isomers determined under closely standardised conditions. Owing to the hygroscopic nature of pyridine and its homologues, it was preferred in the earlier work [1] to calculate the heat of combustion per mole from the mass of carbon dioxide formed. In the present study, however, the more conventional procedure was used of calculating the heat of combustion per mole from the mass of substance burned.

### EXPERIMENTAL

*Materials.*—Samples of 2 : 3-, 3 : 4-, and 3 : 5-lutidine [2] were synthesised, and samples of 2 : 4-, 2 : 5-, and 2 : 6-lutidine were isolated from coal-tar bases,[3] by Dr. E. A. Coulson and his colleagues. Methods of bringing 2 : 6-lutidine to great purity have been described; [4] methods for purifying the others will be given in due course. The purities of the actual specimens employed (in moles %), as determined cryoscopically [5,6] before the intensive drying described below, were: 2 : 3-, 99·65 ± 0·17; 2 : 4-, 99·80 ± 0·10; 2 : 5-, 99·85 ± 0·07; 2 : 6-, 99·89 ± 0·05; 3 : 4-, 99·88 ± 0·06; and 3 : 5-lutidine, 99·74 ± 0·13.

The above purity measurements were made on samples which had been dried by distillation, but infrared spectroscopy [7] disclosed that water was still present in all the samples; indeed, the water contents, as indicated by quantitative spectroscopic analysis, corresponded within experimental error with the total amounts of impurity found cryoscopically, except for the sample of 3 : 5-lutidine where there appeared to be *ca.* 0·2 mole % of impurity other than water.

To determine heats of combustion per mole to an accuracy of 1 part in 10,000 from the mass of liquid burned, the water contents of the samples should not have exceeded 0·01 wt. % = 0·06 mole %. Earlier experience had shown that intensive drying of pyridine bases by many chemical drying agents is attended by the *formation* of impurities, but it has now been established that calcium hydride, which has been successfully used for drying numerous sulphur compounds,[8] is free from this objection. Moreover, calcium hydride is so effective as a drying

* The paper by Cox, Challoner, and Meetham, *J.*, 1954, 265, is regarded as Part I.

[1] Cox, Challoner, and Meetham, *J.*, 1954, 265.
[2] Coulson and Ditcham, *J.*, 1957, 356.
[3] Coulson, Hales, Holt, and Ditcham, *J. Appl. Chem.*, 1952, **2**, 71.
[4] Biddiscombe, Coulson, Handley, and Herington, *J.*, 1954, 1957.
[5] Herington, *Analyt. Chim. Acta*, 1957, **16**, 15.
[6] Handley, *ibid.*, p. 115.
[7] Coulson, Hales, and Herington, *J.*, 1951, 2125.
[8] Reports of the American Petroleum Institute's Project 48, communicated by Dr. G. Waddington.

XUM

agent that the water content of a lutidine stored over powdered calcium hydride for several days is reduced below 0·01 wt. %.

*Filling into Ampoules.*—Samples of the lutidines, dried by standing for at least 3 days over calcium hydride, were dispensed into soda-glass ampoules (mass *ca.* 80 mg.) of the pattern described by Guthrie *et al.*[9] by means of a vacuum apparatus similar to that used by them, except that a glass rack was used to support the ampoules during filling. This consisted of two parallel circular glass plates, one vertically above the other and fused at their centres to a long glass rod. The bottom plate rested on glass lugs fused into the wall of the filling vessel. Each ampoule rested on the upper plate with its stalk projecting down through a hole in each plate, and up to six could be filled at once, after which they were sealed in turn by use of a minute hydrogen flame.[9] The stalks were placed in a vacuum desiccator to remove excess of lutidine, and finally each ampoule with its stalk was weighed; weights calibrated at the National Physical Laboratory were used, and conversion to a vacuum basis was made in the usual way.

*Calorimetry.*—The bomb calorimeter used has been described;[10,11] of the two bombs available, only that of internal volume 0·297 l. was employed. The energy equivalent of the calorimeter containing this bomb was determined electrically[10,11] as 17,275·8 ± 0·9 J/deg. for a standard mass of 10,430·00 g.; very small adjustments to the energy equivalent were made to take account of any departures from the standard mass in individual experiments.

Two important changes in the earlier calorimetric technique[1] were made. (i) The ampoule was burst and its contents were ignited by means of a fuse of *ca.* 10 mg. of Polythene, which was itself ignited by connecting a 6 v supply across a short length of platinum wire[10] (0·1 mm. diam.). The Polythene was in the form of thin rings, cut from tubing, which were hung from the platinum wire so that they touched the top of an ampoule lying in the platinum crucible. A flux-meter in the firing circuit indicated the electrical energy of ignition. (ii) All temperatures were measured with the platinum-resistance thermometer.

*Analysis of Bomb Products.*—The nitric acid formed was determined by titration of the bomb washings with 0·1N-sodium hydroxide solution. Analysis of the bomb gases for carbon dioxide or carbon monoxide was not carried out systematically, although a few checks were made (cf. ref. 1). Earlier experience had indicated that when appreciable amounts of carbon monoxide are present in the bomb gases, patches of soot are invariably to be found in the bomb. Hence, we rejected experiments in which soot was found after combustion (3 out of 41). Experiments in which the characteristic smell of lutidine was detected in the neutralised bomb washings were also rejected (3 further experiments out of 41). Tests showed that 0·1 mg. of a lutidine could thus be unambiguously detected.

*Units and Auxiliary Data.*—The energy equivalent of the calorimeter was determined electrically in absolute joules; conversion into "thermochemical" calories was made by the definition 1 cal. = 4·1840 J. The 1953 international atomic weights were used.[12] The energy of formation of nitric acid from nitrogen, oxygen, and water was taken as −57·8 kJ/mole.[13] Strictly, this value refers to 0·1N-nitric acid, whereas the *average* concentration of nitric acid in the bomb, after combustion of a lutidine sample with 1 g. of water initially in the bomb, was 0·7N. However, since there was no proof that the concentration of nitric acid in the condensed liquid was uniform throughout the bomb, and since also the energy of dilution of nitric acid from 0·7N to 0·1N is very small (*ca.* −0·16 kJ/mole[14]), we preferred to employ the commonly used value for the energy of formation of nitric acid. The energy of combustion of Polythene was measured in 4 experiments as −46·24 ± 0·05 kJ/g. (−11·05 kcal./g.). The enthalpy of formation of liquid water was taken as −285·840 kJ/mole[14] (−68·3174 kcal./mole) and that of gaseous carbon dioxide as −393·513 kJ/mole[14] (−94·0518 kcal./mole).

*Results.*—Values of the measured energy changes for the reactions occurring in the bomb are given in Table 1, which also lists the corrections (all to be subtracted numerically from the measured energy change) for the formation of nitric acid, $-q_{HNO_3}$; for the combustion of Polythene, $-q_p$; for electrical ignition, $-q_{e.i.}$; and for the conversion to the standard state,

[9] Guthrie, Scott, Hubbard, Katz, McCullough, Gross, Williamson, and Waddington, *J. Amer. Chem. Soc.*, 1952, **74**, 4662.
[10] Challoner, Gundry, and Meetham, *Phil. Trans.*, 1955, **247**, 553.
[11] Gundry and Meetham, to be published.
[12] *J.*, 1954, 4713.
[13] Rossini, "Experimental Thermochemistry," Interscience, New York, 1956, p. 142.
[14] "Selected Values of Chemical Thermodynamic Properties," National Bureau of Standards Circular 500, Washington, 1952.

$-q_{s.s.}$; the last correction was calculated by the method previously given.[1] The corrected temperature rises in Table 1 were calculated according to ref. 10. In order to avoid the tedium of making a separate standard-state correction for the Polythene fuse, the empirical formula of the lutidine was weighted to take account of the Polythene employed. The very small correction for the disappearance of reactants and the appearance of products, which

TABLE 1.

| Compound | Mass (g.) | Temp. rise (corr.) (° c) | Heat evolved (J) | $-q_{HNO_3}$ (J) | $-q_p$ (J) | $-q_{s.i.}$ (J) | $-q_{s.s.}$ (J) | $-\Delta U_c°$ (kJ/mole) |
|---|---|---|---|---|---|---|---|---|
| 2 : 3-Lutidine | 0·96756 | 2·15315 | 37210·9 | 64·6 | 495·3 | 0·5 | 18·8 | 4056·7 |
| | 0·89372 | 1·99149 | 34420·5 | 67·7 | 508·8 | 0·5 | 17·1 | 4055·5 |
| | 1·10340 | 2·44732 | 42300·6 | 86·2 | 410·0 | 0·8 | 21·9 | 4057·4 |
| | 0·86936 | 1·93607 | 33459·4 | 55·1 | 484·3 | 0·5 | 16·6 | 4055·3 |
| | 0·89376 | 1·98776 | 34355·3 | 61·7 | 461·4 | 0·7 | 17·1 | 4053·9 |
| | | | | | | | Average | 4055·8 |
| 2 : 4-Lutidine | 0·69762 | 1·55835 | 26932·4 | 47·1 | 490·1 | 0·6 | 12·8 | 4052·1 |
| | 0·66033 | 1·47640 | 25516·8 | 51·0 | 476·2 | 0·6 | 12·1 | 4052·9 |
| | 0·75690 | 1·69133 | 29231·3 | 52·8 | 527·0 | 0·6 | 14·2 | 4053·9 |
| | 0·68857 | 1·53870 | 26594·3 | 51·5 | 488·4 | 0·6 | 12·7 | 4052·3 |
| | 0·61762 | 1·38416 | 23921·1 | 50·1 | 504·5 | 0·6 | 11·2 | 4051·8 |
| | 0·75734 | 1·68802 | 29172·4 | 50·6 | 464·6 | 0·6 | 14·1 | 4052·4 |
| | | | | | | | Average | 4052·6 |
| 2 : 5-Lutidine | 0·52145 | 1·17260 | 20266·1 | 43·7 | 478·8 | 0·6 | 9·3 | 4055·0 |
| | 0·55700 | 1·25061 | 21614·3 | 43·2 | 478·9 | 0·5 | 10·0 | 4055·5 |
| | 0·55968 | 1·25640 | 21714·7 | 45·7 | 478·9 | 0·5 | 10·0 | 4054·8 |
| | 0·56072 | 1·25738 | 21732·3 | 44·2 | 463·4 | 0·6 | 10·0 | 4053·9 |
| | 0·82488 | 1·84345 | 31860·9 | 63·7 | 554·5 | 0·7 | 15·6 | 4056·2 |
| | | | | | | | Average | 4055·1 |
| 2 : 6-Lutidine | 0·70309 | 1·56972 | 27130·1 | 53·8 | 473·9 | 0·6 | 12·9 | 4052·1 |
| | 0·53846 | 1·20845 | 20883·5 | 45·2 | 479·2 | 0·5 | 9·6 | 4049·3 |
| | 0·65075 | 1·45382 | 25123·8 | 49·0 | 490·2 | 0·5 | 11·9 | 4046·0 |
| | 0·68893 | 1·53794 | 26578·6 | 47·0 | 478·8 | 0·7 | 12·7 | 4049·9 |
| | 0·64512 | 1·44075 | 24899·5 | 48·2 | 463·4 | 0·6 | 11·8 | 4048·6 |
| | 0·84517 | 1·87623 | 32429·4 | 55·6 | 421·8 | 0·8 | 16·2 | 4048·7 |
| | 0·90899 | 2·02126 | 34934·7 | 66·9 | 498·7 | 0·6 | 17·5 | 4049·2 |
| | | | | | | | Average | 4049·1 |
| 3 : 4-Lutidine | 0·86508 | 1·92806 | 33319·9 | 67·7 | 487·1 | 0·6 | 16·5 | 4056·2 |
| | 0·73064 | 1·63432 | 28243·9 | 48·7 | 535·8 | 0·5 | 13·5 | 4054·3 |
| | 0·85508 | 1·90657 | 32950·5 | 60·0 | 515·8 | 0·5 | 16·3 | 4054·8 |
| | 0·78178 | 1·74413 | 30142·1 | 59·9 | 497·7 | 0·6 | 14·7 | 4052·7 |
| | 0·79351 | 1·76989 | 30589·4 | 63·0 | 478·9 | 0·6 | 14·9 | 4055·3 |
| | 0·85812 | 1·90644 | 32949·9 | 60·0 | 399·1 | 0·5 | 16·3 | 4054·9 |
| | | | | | | | Average | 4054·7 |
| 3 : 5-Lutidine | 0·72811 | 1·63002 | 28172·6 | 52·8 | 532·2 | 0·5 | 13·5 | 4057·8 |
| | 0·82643 | 1·84724 | 31926·7 | 58·0 | 543·8 | 0·6 | 15·6 | 4059·3 |
| | 0·72679 | 1·62852 | 28142·9 | 54·0 | 533·5 | 0·6 | 13·5 | 4060·4 |
| | 0·77995 | 1·74702 | 30192·9 | 64·4 | 567·7 | 0·5 | 14·7 | 4059·0 |
| | 0·74800 | 1·66828 | 28831·9 | 48·5 | 437·7 | 0·5 | 13·9 | 4058·4 |
| | 0·84777 | 1·89427 | 32738·1 | 59·7 | 551·1 | 0·6 | 16·1 | 4058·5 |
| | | | | | | | Average | 4058·9 |

Washburn [15] called the "isothermal correction," was made separately from the standard-state correction; after application of this correction the values given in col. 4 of Table 1 were obtained. The final column of Table 1 gives values of the energy change, $-\Delta U_c°$, for the following combustion reaction at 25°: $C_7H_9N$ (liq.) + $37/4O_2$ ⟶ $7CO_2$ + $9/2H_2O$ (liq.) + $\frac{1}{2}N_2$.

## DISCUSSION

Mean values of $\Delta U_c°$, $\Delta H_c°$, and $\Delta H_f°$ for the liquid state are presented in Table 2 (where all values are given in kcal./mole), together with the standard deviations of the mean. Comparison of these standard errors with those in Table 2 of ref. 1 reveals that the precision of the present work is somewhat the greater, probably due to some or all of the following improvements: (i) only one bomb was used, (ii) temperatures were measured

[15] Washburn, *J. Res. Nat. Bur. Stand.*, 1933, **10**, 525.

by a platinum-resistance thermometer, (iii) the heat of combustion per mole was calculated directly from the mass of sample taken, (iv) rejection of experiments on suspicion of poor combustion was more rigorous.

TABLE 2.

| Lutidine | $\Delta U_c°$ | $\Delta H_c°$ | $\Delta H_f°$ | $\sigma_1$ * | $\sigma_2$ † | Lutidine | $\Delta U_c°$ | $\Delta H_c°$ | $\Delta H_f°$ | $\sigma_1$ * | $\sigma_2$ † |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 : 3- | −969·36 | −970·40 | +4·61 | 0·14 | 0·15 | 2 : 6- | −967·76 | −968·80 | +3·01 | 0·17 | 0·18 |
| 2 : 4- | −968·59 | −969·63 | +3·84 | 0·08 | 0·09 | 3 : 4- | −969·10 | −970·14 | +4·35 | 0·11 | 0·12 |
| 2 : 5- | −969·19 | −970·23 | +4·44 | 0·10 | 0·11 | 3 : 5- | −970·10 | −971·14 | +5·35 | 0·09 | 0·10 |

* $\sigma_1$ is the standard deviation of the mean value of $\Delta U_c°$ *without* considering the standard error of the energy equivalent of the calorimeter; it should be used when making internal comparison within the lutidine series, *e.g.*, for deriving heats of isomerisation. $\sigma_1$ also applies to values of $\Delta H_c°$ and $\Delta H_f°$ for purposes of internal comparison.

† $\sigma_2$ is the standard deviation of the mean value of $\Delta U_c°$ (or $\Delta H_c°$, or $\Delta H_f°$) when the standard error of the energy equivalent of the calorimeter is considered; it should be used for making comparisons with other work.

The problem of *systematic* errors was discussed earlier[1] under five headings. The first does not apply to the present work, since the heats of combustion per mole are no longer based on the mass of carbon dioxide formed, whilst the issue discussed under the fifth heading, concerning the difference between electrical-heating and combustion experiments, has since been resolved.[10] Of the remaining systematic errors, probably those due to impurities in the samples are alone appreciable.

Values of $\Delta U_c°$ for 2 : 5- and 2 : 6-lutidine were given earlier,[1] and comparison with the present values reveals close agreement for 2 : 5-lutidine but less close agreement for 2 : 6-lutidine; however, the difference between the present and earlier values in the latter instance is not statistically significant, having regard to the known standard errors. The present value is to be preferred, not merely because the reproducibility error is smaller, but also because the systematic errors are thought to be smaller. Values of the heats of formation of all the lutidines in the ideal-gas state cannot yet be given because latent heats of vaporisation at 25° and second virial coefficients are available only for 2 : 6-lutidine,[16] although it is hoped that data for the other lutidines will be available later.

The difference between values of $\Delta H_c°$ for any pair of lutidines corresponds to the heat of isomerisation of one to the other, $\Delta H_i°$, in the liquid state. Thus, the following values were deduced from Table 2:

| $\Delta H_i°$ (kcal./mole) for | | $\Delta H_i°$ (kcal./mole) for | |
|---|---|---|---|
| 2 : 6- ⟶ 2 : 4-Lutidine, | + 0·84 ± 0·19 | 2 : 6- ⟶ 2 : 3-Lutidine, | + 1·60 ± 0·22 |
| 2 : 6- ⟶ 3 : 4-Lutidine, | + 1·34 ± 0·20 | 2 : 6- ⟶ 3 : 5-Lutidine, | + 2·34 ± 0·19 |
| 2 : 6- ⟶ 2 : 5-Lutidine, | + 1·43 ± 0·20 | | |

These heats of isomerisation are considerably greater in magnitude than those in the structurally similar xylene series, where $\Delta H_i°$ (liquid state) for *m*- ⟶ *o*-xylene and for *m*- ⟶ *p*-xylene is +0·24[17] to +0·45[18] kcal./mole. Values of $\Delta H_c°$ for the xylenes in the *gas* state are also numerically small (<0·5 kcal./mole), but until latent heats of vaporisation and second virial coefficients are available for all the lutidines it cannot be decided whether the relatively large heats of isomerisation of the lutidines are due to differences in resonance energy or in liquid structure.

We acknowledge the help given by Dr. E. A. Coulson in providing the lutidine samples, by Dr. E. F. G. Herington and Mr. D. Harrop in making the purity measurements, and by Mr. D. E. Pinnock in rendering technical assistance. This work formed part of a joint programme by the Chemical Research Laboratory and the National Physical Laboratory and is published by permission of the Directors of the two Laboratories.

CHEMICAL RESEARCH LABORATORY, D.S.I.R., TEDDINGTON, MIDDLESEX.
NATIONAL PHYSICAL LABORATORY, TEDDINGTON, MIDDLESEX. [*Received, September 2nd*, 1957.]

[16] Andon, Cox, Herington, and Martin, *Trans. Faraday Soc.*, 1957, **53**, 1074.
[17] Prosen, Gilmont, and Rossini, *J. Res. Nat. Bur. Stand.*, 1945, **34**, 259, 263.
[18] Coops, Mulder, Dienske, and Smittenberg, *Rec. Trav. chim.*, 1946, **65**, 128.

## 205. *Structure and Properties of Mesomeric Systems. Part I. Resonance Energies.*

By David Peters.

A simple perturbation method is used to derive the Hückel resonance energies of a large number of mesomeric hydrocarbons from the resonance energies of the corresponding straight-chain polyenes.

The Hückel L.C.A.O. molecular-orbital method,[1] despite its shortcomings,[2] remains the only one of wide applicability in problems of structure, chemical reactivity, and ultraviolet spectra of mesomeric systems. The more sophisticated methods, successful though they are with a small group of molecules, fail to provide the organic chemist with the versatile method required in practice. The Hückel method itself, however, is not always free from arithmetical complexity and there is now described a perturbation method whereby the resonance energy of mesomeric hydrocarbons can be determined with a minimum of labour.

Conceptually, the method is derived from Dewar and Pettit's demonstration [3] that the properties of mesomeric hydrocarbons can be derived from those of the cyclic polyenes, the formation of the cross-links being treated as a perturbation. The latter method is limited, however, in that the highly condensed benzenoid hydrocarbons (pyrene, perylene, and coronene), the vinyl substituted benzenoids (styrene, stilbene), and the non-alternant hydrocarbons having exocyclic bonds (fulvene, fulvalene) are all outside of its scope. A simple method for the hydrocarbons of the last category would be particularly useful owing to the complexity of their normal secular equations. Lacking symmetry, such hydrocarbons present formidable problems in calculation.

A variant on Dewar and Pettit's cyclic-polyene method is now described, the properties of the mesomeric hydrocarbons being derived from those of the open-chain linear polyenes. Most hydrocarbons in the above three classes then come within range, the few exceptions being listed below. Perturbation methods, in addition to eliminating the labour involved in computation, also bring out relations between classes of hydrocarbons which are less evident from the results obtained by solution of the secular equations.

*Method.*—The mathematical properties of the linear polyenes, investigated by Lennard-Jones [4] and by Coulson,[5] are required. The energy ($e_j$) of the $j$th molecular orbital ($\psi_j$) of a linear polyene ($C_nH_{n+2}$) is given [1] by

$$e_j = 2\beta \cos [j\pi/(n+1)], j = 1, 2, \ldots . n \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and the atomic-orbital coefficient ($c_{rj}$) of the $j$th molecular orbital at the $r$th carbon atom by

$$c_{rj} = [2/(n+1)]^{\frac{1}{2}} \sin [rj\pi/(n+1)] \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The occupied molecular orbitals are $j = 1, 2 \ldots . n/2$ and $\beta$ is the standard carbon–carbon bond resonance integral, overlap being neglected.

Now consider the formation of a cross-link between atoms $r$ and $s$. Denote the change in the Hamiltonian of the system by $\delta H$ and the energy of the perturbed $j$th molecular-orbital by $e_j'$, then first-order perturbation theory gives

$$e_j' = e_j + \int \psi_j \, . \, \delta H \, . \, \psi_j \, . \, d\tau \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

[1] Hückel, *Z. Physik*, 1930, **60**, 423; 1931, **70**, 204; 1931, **72**, 310; 1932, **76**, 628.
[2] Coulson and Dewar, *Discuss. Faraday Soc.*, 1947, **2**, 54.
[3] Dewar and Pettit, *J.*, 1954, 1617.
[4] Lennard-Jones, *Proc. Roy. Soc.*, 1937, *A*, **158**, 280.
[5] Coulson, *ibid.*, 1938, *A*, **164**, 383.

XUM

Expand the $\psi_j$'s in terms of the constituent atomic orbitals ($\phi_s$) from $\sum_r c_{rj} \cdot \phi_r = \psi_j$ and suppose that the only non-vanishing terms in the expansion are $\phi_r \cdot \delta H \cdot \phi_s(\beta_{rs})$ [3, 6, 7] then

$$e_j' = e_j + 2c_{rj}c_{sj} \cdot \beta_{rs} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

*i.e.*,

$$E_a = 2\sum^{occ} e_j' = E_{l.p.} + 4\beta \sum_{j=1-(n/2)} \cdot c_{rj}c_{sj} \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where $E_{l.p.}$ and $E_a$ are the total $\pi$-electron energies of the linear polyene and the cross-linked polyene (aromatic) respectively. All $\beta$'s are taken equal. From eqns. (2) and (5)

$$E_a = E_{l.p.} + \frac{8\beta}{n+1} \sum_{j=1-(n/2)} \left( \sin \frac{rj\pi}{n+1} \cdot \sin \frac{sj\pi}{n+1} \right) \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$= E_{l.p.} + \frac{4\beta}{n+1} \sum_{j=1-(n/2)} \left( \cos \frac{(r-s)j\pi}{n+1} - \cos \frac{(r+s)j\pi}{n+1} \right) \quad . \quad . \quad . \quad (7)$$

and since

$$\sum_{p=1-q} \cos(p\theta) = \sin\left[(q+\tfrac{1}{2})\theta\right] \Big/ \left(2\sin\frac{\theta}{2}\right) - \tfrac{1}{2} \quad . \quad . \quad . \quad . \quad . \quad (8)$$

$$E_a = E_{l.p.} + \frac{2\beta}{n+1}\left( \frac{\sin[(r-s)\pi/2]}{\sin\{(r-s)\pi/[2(n+1)]\}} - \frac{\sin[(r+s)\pi/2]}{\sin\{(r+s)\pi/[2(n+1)]\}} \right) . \quad (9)$$

First-order perturbations being additive, the formation of several cross-links is given by the sum of each determined from eqn. (9).

Before we proceed to explicit calculations, certain interesting general results can be obtained from eqn. (9). If $(r-s)$ and $(r+s)$ are even integers, the expression in large parentheses vanishes for all such values of $r$, $s$, and $n$. Physically, this means that cross-linking of atoms of like parity * does not change the $\pi$-electron energy of the system (see p. 1027). The $(4\gamma+2)$ rule of aromaticity [1] can also be deduced from eqn. (9) as follows. First consider the denominators in the term in braces. Both $(r-s)$ and $(r+s)$ are less than $2(n+1)$ and both denominators are thus positive. Now let $s=1$. If $r=(4\gamma+2)$, then $(r-s)=4\gamma+1$ and the first sine term in the braces is positive, the second negative. The resonance energy is thus high. When $r=4\gamma$, however, it is easily seen that the first sine term is negative, the second positive, and the resonance energy is low.

The $\pi$-electron energy ($E_{l.p.}$) of the polyene must be computed. From eqn. (1),

$$E_{l.p.} = 4\beta \sum_{j=1-(n/2)} \cos[j\pi/[n+1)] \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

$$= 2\beta \operatorname{cosec}\{\pi/[2(n+1)]\} - 2\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

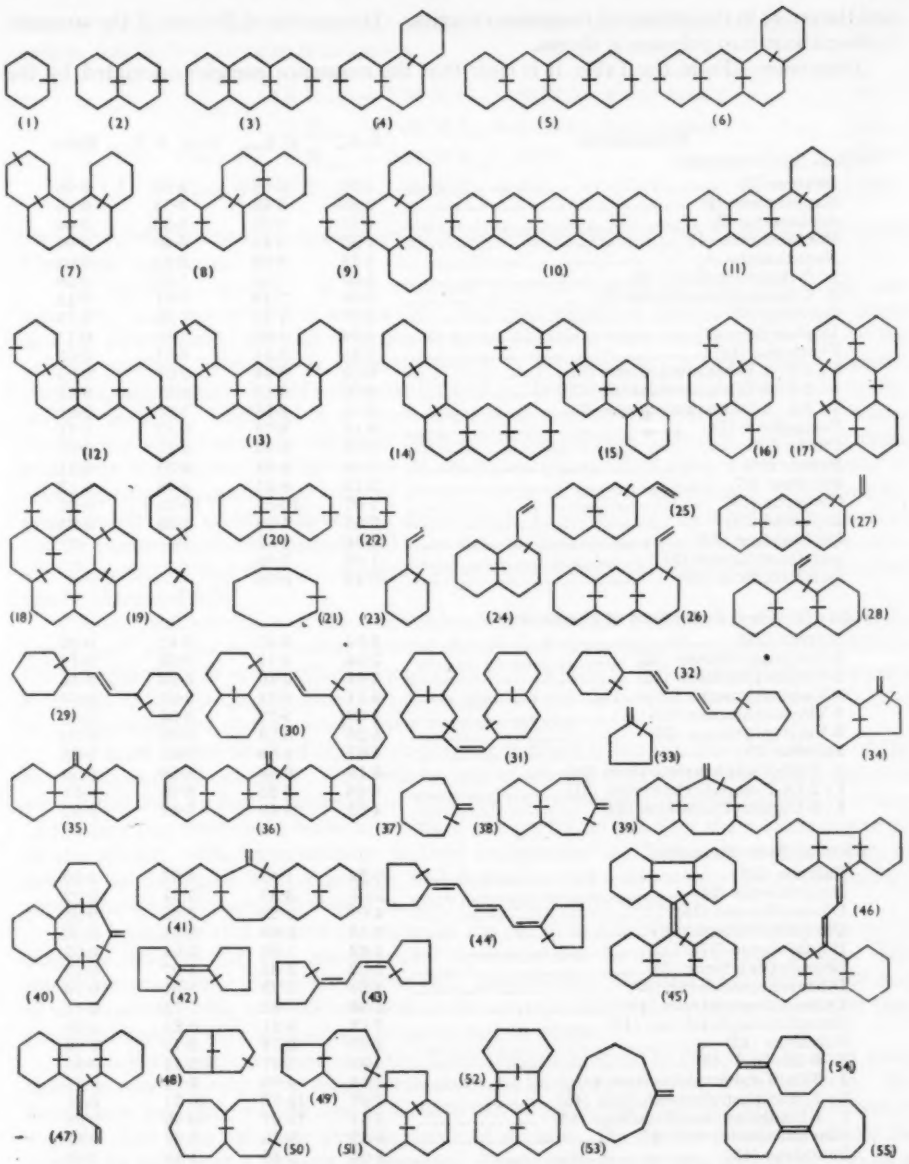
The resonance energy of the cross-linked aromatic hydrocarbon is then

$$\text{R.E}_a. = 2\beta \operatorname{cosec}\{\pi/[2(n+1)]\} - (n+2)\beta + \frac{2\beta}{n+1}\left( \frac{\sin[(r-s)\pi/2]}{\sin\{(r-s)\pi/[2(n+1)]\}} - \frac{\sin[(r+s)\pi/2]}{\sin\{(r+s)\pi/[2(n+1)]\}} \right) . \quad (12)$$

It is convenient to classify the mesomeric hydrocarbons in three groups: (*a*) alternants,

* Atoms are of like parity when both are starred or unstarred.

[6] Longuet-Higgins and Sowden, *J.*, 1952, 1404.
[7] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341.




**All these compounds are formally aromatic, although the double bonds are omitted for convenience. The cross-lines represent the points at which the rings are regarded as being "closed" from the linear polyenes.**

(*b*) vinyl derivatives of alternants, (*c*) non-alternants. In the Table (all quantities in units of β) are listed the resonance energies ($R.E._a$) calculated by the perturbation methods [eqn. (12)], the resonance energies ($R.E._{s.e.}$) obtained by solution of the secular equations,[8]

[8] Pullman and Pullman, "Les Théories Electroniques de la Chimie Organique," Masson et Cie., Paris, 1952, p. 226; p. 632 *et seq.*

and the errors in the estimated resonance energies. The manner of division of the aromatic hydrocarbons into polyenes is shown.

*Discussion.*—From the Table, it is clear that the resonance energies calculated by the

| Hydrocarbon | R.E.$_a$ | R.E.$_{s.e.}$ | Corr. R.E. | Error |
|---|---|---|---|---|
| *Class* (*a*) (alternants). | | | | |
| Benzene (1) | 1·59 | 2·00 | 2·00 | 0·00 |
| Naphthalene (2) | 2·88 | 3·68 | 3·73 | 0·05 |
| Anthracene (3) | 4·10 | 5·31 | 5·36 | 0·05 |
| Phenanthrene (4) | 3·83 | 5·45 | 5·40 | 0·05 |
| Naphthacene (5) | 5·28 | 6·93 | 6·94 | 0·01 |
| 1 : 2-Benzanthracene (6) | 5·07 | 7·10 | 7·30 | 0·20 |
| 3 : 4-Benzophenanthrene (7) | 5·08 | 7·19 | 7·31 | 0·12 |
| Chrysene (8) | 5·07 | 7·19 | 7·30 | 0·11 |
| Triphenylene (9) | 4·94 | 7·27 | 7·10 | 0·17 |
| Pentacene (10) | 6·45 | 8·54 | 8·51 | 0·03 |
| 1 : 2-3 : 4-Dibenzanthracene (11) | 6·19 | 8·94 | 9·01 | 0·07 |
| 1 : 2-5 : 6-Dibenzanthracene (12) | 6·10 | 8·88 | 8·87 | 0·01 |
| 1 : 2-7 : 8-Dibenzanthracene (13) | 6·10 | 8·88 | 8·87 | 0·01 |
| Pentaphene (14) | 6·10 | 8·76 | 8·87 | 0·11 |
| Picene (15) | 6·10 | 8·94 | 8·87 | 0·07 |
| Pyrene (16) | 4·55 | 6·51 | 6·50 | 0·01 |
| Perylene (17) | 5·78 | 8·25 | 8·38 | 0·13 |
| Coronene (18) | 7·07 | 10·57 | 10·35 | 0·22 |
| Diphenyl (19) | 3·55 | 4·38 | 4·63 | 0·25 |
| Diphenylene (20) | 2·04 | 4·51 | — | — |
| *cyclo*Octatetraene (21) | 1·06 | 1·66 | — | — |
| *cyclo*Butadiene (22) | −0·42 | 0·00 | — | — |
| *Class* (*b*) (vinyl derivatives of alternants). | | | | |
| Styrene (23) | 2·04 | 2·42 | 2·42 | 0·00 |
| 1-Vinylnaphthalene (24) | 3·04 | 4·12 | 3·99 | 0·13 |
| 2-Vinylnaphthalene (25) | 3·02 | 4·10 | 3·96 | 0·14 |
| 1-Vinylanthracene (26) | 4·11 | 5·74 | 5·67 | 0·07 |
| 2-Vinylanthracene (27) | 4·09 | 5·72 | 5·64 | 0·08 |
| 9-Vinylanthracene (28) | 4·25 | 5·79 | 5·89 | 0·10 |
| Stilbene (29) | 4·07 | 4·88 | 5·61 | 0·73 |
| 1 : 2-Di-1′-naphthylethylene (30) | 6·16 | 8·30 | 8·89 | 0·59 |
| 1 : 2-Di-2′-naphthylethylene (31) | 6·08 | 8·25 | 8·76 | 0·51 |
| 1 : 4-Diphenylbutadiene (32) | 4·59 | 5·40 | 6·42 | 1·02 |
| *Class* (*c*) (non-alternants). | | | | |
| Fulvene (33) | 0·99 | 1·47 | 1·37 | 0·10 |
| Benzofulvene (34) | 2·51 | 3·33 | 3·31 | 0·02 |
| Dibenzofulvene (35) | 4·01 | 5·22 | 5·23 | 0·01 |
| Dinaphthofulvene (36) | 6·59 | 8·60 | 8·54 | 0·06 |
| Heptafulvene (37) | 1·52 | 1·99 | 2·04 | 0·05 |
| Benzoheptafulvene (38) | 3·02 | 3·84 | 3·97 | 0·13 |
| Dibenzoheptafulvene (39) | 4·54 | 5·73 | 5·91 | 0·18 |
| Tribenzoheptafulvene (40) | 5·96 | 7·62 | 7·73 | 0·11 |
| Dinaphthoheptafulvene (41) | 7·12 | 9·41 | 9·21 | 0·20 |
| Fulvalene (42) | 2·05 | 2·78 | 2·72 | 0·06 |
| Di-6-fulvenyl (43) | 2·59 | 3·47 | 3·42 | 0·05 |
| 1 : 2-Di-6′-fulvenylethylene (44) | 3·13 | 4·09 | 4·10 | 0·01 |
| 1 : 2-Bisdiphenylene-ethylene (45) | 7·97 | 10·52 | 10·31 | 0·21 |
| 1 : 4-Bisdiphenylenebutadiene (46) | 8·51 | 11·07 | 10·99 | 0·08 |
| Vinyldibenzofulvene (47) | 4·52 | 5·76 | 5·88 | 0·12 |
| Pentalene (48) | 1·06 | 2·46 | 1·46 | 1·00 |
| Azulene (49) | 2·42 | 3·36 | 3·20 | 0·16 |
| Heptalene (50) | 2·28 | 3·62 | 3·02 | 0·60 |
| Acenaphthylene (51) | 3·40 | 4·62 | 4·45 | 0·17 |
| Fluoranthene (52) | 4·89 | 6·50 | 6·36 | 0·14 |

perturbation method differ from those calculated from the secular equations. Nevertheless, there is a linear relation between the two sets of resonance energies, and this is the same situation as that found by Dewar and Pettit [3] in their cyclic-polyene method.

Greater accuracy is possible if slightly different equations are used for each class of hydrocarbon and the best straight lines are:

$$\text{Class } (a)\begin{cases}\text{R.E.}_{\text{s.e.}} = 1{\cdot}34\ \text{R.E.}_{\text{s}} - 0{\cdot}13 \text{ for linear acenes} & (13)\\ \text{R.E.}_{\text{s.e.}} = 1{\cdot}53\ \text{R.E.}_{\text{s}} - 0{\cdot}46 \text{ for bent acenes} & (14)\end{cases}$$

$$\text{Class } (b)\quad \text{R.E.}_{\text{s.e.}} = 1{\cdot}57\ \text{R.E.}_{\text{s}} - 0{\cdot}78 \quad (15)$$

$$\text{Class } (c)\quad \text{R.E.}_{\text{s.e.}} = 1{\cdot}28\ \text{R.E.}_{\text{s}} + 0{\cdot}1 \quad (16)$$

The corrected resonance energies reported in the fourth column of the Table are calculated from these equations.

The resonance energies of the common benzenoid hydrocarbons containing six-membered rings are estimated accurately. Different equations are required for the linear and the bent acenes, and this situation is again identical with that found in the cyclic-polyene method. Benzene is correctly found to be common to both lines. Pyrene, perylene, and coronene are of particular interest as they cannot be reached with the cyclic-polyene method. Diphenyl is a representative of another class of hydrocarbon whose resonance energy cannot be obtained from the cyclic-polyene approach, and the current treatment is of immediate interest for its analogues (dinaphthyl, etc.) where symmetry is rarely of help in reducing the order of the conventional secular equations. The points for *cyclo*octatetraene, *cyclo*butadiene, and diphenylene do not fall on the same line as those of the six-membered ring compounds and more data on the secular equation resonance energies of compounds of this type are required before the reliability of the perturbation method can be examined fully.

The resonance energies of the vinyl-substituted aromatic hydrocarbons are accurately reproduced and the perturbation method should find immediate application in predicting the position of Diels–Alder attack in molecules of this kind.[9] The disubstituted ethylenes evidently require a characteristic line since they do not fall on the line generated by the vinyl hydrocarbons, as is shown by their large deviations.

The most useful result of the linear-polyene method is the excellent behaviour of the non-alternant hydrocarbons. The tedious task of solving their secular equations can now be avoided and, in fact, calculation of their resonance energies is particularly easy owing to the fact that cross-links between atoms of like parity do not alter the π-electron energy of the system. The linear-polyene method exaggerates the higher resonance energy of azulene as compared with pentalene and heptalene but fortunately the cyclic-polyene method is available here and should be used for quantitative work.

It is noticeable that no rule analogous to the $(4\gamma + 2)$ rule of aromaticity for the cyclic polyenes emerges for the non-alternant hydrocarbons having exocyclic bonds. The resonance energies of the series fulvene (**33**), heptafulvene (**37**), and nonafulvene (**53**) and of the series (**42**), (**54**), and (**55**) are those of the corresponding open-chain polyenes and thus increase regularly with increasing number of carbon atoms.

There is a possibly ambiguity in the linear-polyene method in that there is often more than one way of dividing the cross-linked aromatic hydrocarbon into a linear polyene. No formal rule governing the manner of division can be given but when the larger members of a given class have only one possible mode of division, the smaller members should be divided in as similar a manner as possible. When only one or two representatives of a given type of hydrocarbon are known (*e.g.*, acenaphthylene, fluoranthene) the results must be accepted with caution until the reliability of the perturbation method can be checked on a larger number of representatives.

It is not, of course, correct to infer that the equality of the resonance energies of some of the non-alternant hydrocarbons and the corresponding cyclic or linear polyene leads to equality of chemical reactivity. The ability of these non-alternant hydrocarbons to be

[9] R. D. Brown, *J.*, 1950, 691, 2730; 1951, 1612, 3129.

prepared is primarily a function of their chemical reactivity, and there is no simple connection between the latter property and the resonance energy. The point is taken up in detail in the following paper.

For obvious geometric reasons, certain mesomeric hydrocarbons are outside the scope of both the cyclic and the linear polyene methods. The more numerous of these exceptions are hydrocarbons containing either rings having more than one exocyclic bond, the exocyclic bonds not being joined elsewhere in the molecule (*e.g.*, *m*- and *p*-terphenyl), or a carbon atom bonded to three other carbon atoms not joined elsewhere in the molecule (*e.g.*, 1 : 1-diphenylethylene). These exceptions are comparatively unimportant and are not examined further.

The author is indebted to Professor M. J. S. Dewar for advice.

ROYAL HOLLOWAY COLLEGE, ENGLEFIELD GREEN, SURREY. [*Received, September 27th*, 1957.]

---

## 206. *Structure and Properties of Mesomeric Systems. Part II.* The Chemical Reactivity of Alternant and Non-alternant Hydrocarbons.*

By DAVID PETERS.

The chemical reactivity of the purely cyclic alternant and non-alternant hydrocarbons is examined by use of a perturbation method based on the Hückel L.C.A.O. molecular-orbital theory. Atom localisation energies for free-radical and ionic attack and bond localisation energies are obtained for the common benzenoid hydrocarbons and for the cyclic non-alternant hydrocarbons. Agreement between the perturbation localisation energies and those obtained by solution of the secular equation is generally good. The chemical reactivity of a number of complex non-alternant hydrocarbons is examined.

APPLICATION of the Hückel molecular-orbital method [1] to mesomeric hydrocarbons leads to the division of the latter into two classes, the alternant and the non-alternant hydrocarbons.[2] The first class, of which the common benzenoid hydrocarbons are the best known representatives, has been explored extensively, both theoretically and practically.[3] The second has received relatively little attention,[4] owing to the fact that attempts to prepare many of the simple representatives have so far failed. If suitable syntheses can be devised, however, these hydrocarbons should exhibit novel properties, and they will also provide excellent tests for theories of chemical reactivity. One feature of the non-alternant hydrocarbons, their uneven charge distribution, is particularly interesting for in this they may be regarded as intermediate between the hydrocarbons and the heterocycles, and an understanding of their chemistry may be of assistance in solving the difficult problem of the latter compounds.

Theoretical methods are also of potential value in the preparation of non-alternant hydrocarbons. Although it is often assumed that the resonance energies are important in determining the " stability "—and hence of the ability to be prepared—of a hydrocarbon, a better guide to " stability " is the chemical reactivity of the desired hydrocarbon and of the intermediates involved in its synthesis.† The major point of difference between the

* Part I, preceding paper.

† The isolation of diphenylene[5] is then unexceptional since R. D. Brown's theoretical predictions [6] suggest that it is of low chemical reactivity.

[1] Hückel, *Z. Physik*, (*a*) 1931, **70**, 204; (*b*) 1931, **72**, 310; (*c*) 1932, **76**, 628.

[2] (*a*) Coulson and Rushbrooke, *Proc. Camb. Phil. Soc.*, 1940, **36**, 193; (*b*) Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, *A*, **191**, 39; 1947, *A*, **192**, 16; (*c*) Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 265.

[3] Pullman and Pullman, " Les Théories Electroniques de la Chimie Organique," Masson et Cie., Paris, 1952.

[4] Baker and McOmie, " Progress in Organic Chemistry," Vol. 3, ch. 2, Butterworths Scientific Publications, London, 1955.

[5] Lothrop, *J. Amer. Chem. Soc.*, 1941, **63**, 1187.

[6] R. D. Brown, *Trans. Faraday Soc.*, 1950, **46**, 146.

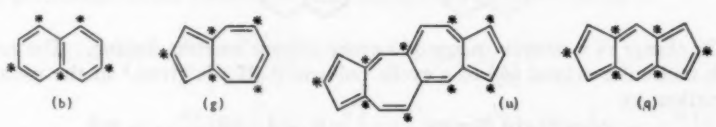
alternant and the non-alternant hydrocarbons is the fact that, in the alternant ones, the π-electron energy of activation is identical for free-radical and for ionic substitution, while this is far from being the case with the non-alternant hydrocarbons in which differences probably corresponding to many powers of ten in the rate occur in the π-electron energies of localisation and some of the non-alternant hydrocarbons may prove to be quite unstable to acid or base. An examination of the theoretical predictions of the reactivity will then provide a useful guide to the reaction conditions which can safely be used in the synthesis.

One disadvantage of the Hückel theory in its original form, particularly for the non-alternant hydrocarbons, is the amount of labour involved in the calculations. Perturbation methods are then very attractive and have the added advantage that they often provide insight into the relations between classes of hydrocarbon. Elegant perturbation methods have been used for the chemical reactivity of the alternant hydrocarbons by Dewar,[7] but these cannot readily be extended to the non-alternant hydrocarbons and other methods have now been developed which provide a simple insight into the properties of the latter. The chemical reactivity of the alternant and non-alternant hydrocarbons is now examined by use of perturbation methods based on the Hückel L.C.A.O. molecular-orbital theory. The basis of the method is the demonstration (preceding paper) that the π energy of mesomeric hydrocarbons may be estimated by regarding them as cross-linked polyenes. When this is extended to polyene radicals, the π energy of the transition state is accessible.

The non-alternant hydrocarbons are themselves divisible into two classes, those containing only rings and those containing exocyclic bonds. Representatives of the former class are pentalene (f), azulene (g), and heptalene (h), and of the latter class fulvene, heptafulvene, and fulvalene. This geometrical difference requires that different treatments be given to the two classes and only the purely cyclic hydrocarbons will be examined here.

We are interested in substitution in, and addition to, mesomeric systems. For this reaction, Wheland's original postulate [8] of the structure of the transition state, in which the reacting carbon atom is completely tetrahedral, is commonly used.[3] Recent work [9] has exposed the inadequacies of this model and current evidence and opinion [10,11] are that the transition state may be anywhere between almost unchanged $sp^2$ and complete $sp^3$, depending on the attacking species and the substrate. Experimental evidence obtained by Dewar *et al.*[11] shows that this variation may be accommodated by treating the resonance integral between the attached carbon atom and its neighbours as an empirical parameter.

In view of its importance to this paper, the starring process [2,7] which distinguishes between alternant and non-alternant systems is reiterated as follows. Choose any carbon atom in a mesomeric hydrocarbon and mark it with a star. Starting from this carbon atom, star alternant carbon atoms throughout the molecule. If this process can be carried to completion, all atoms then being adjacent to atoms of the opposite kind (parity), the hydrocarbon is described as alternant. If, when the staring is complete, two adjacent carbon atoms are of the same parity, the hydrocarbon is non-alternant. Thus naphthalene (b) is alternant and azulene (g) is non-alternant.




One possible source of error should be noted. It is true for the simpler hydrocarbons that an odd-numbered ring is the result of cross-linking atoms of like parity, while an even-numbered ring is formed by cross-linking atoms of opposite parity. This result is

[7] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341 *et seq.*
[8] Wheland, *ibid.*, 1942, **64**, 900.
[9] Melander, *Arkiv Kemi*, 1950, 213.
[10] Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 334.
[11] Dewar, Mole, and Warford, *J.*, 1956, 3581, and refs. therein.

not general if more than two rings are present. In the hydrocarbon (u) for example, the fact that all rings are odd numbered may suggest that all cross-links are between atoms of like parity, but the starring exposes the fallacy. Conversely, in hydrocarbon (q) the presence of a six-membered ring suggests that a cross-link between atoms of opposite parity is present, but starring shows that this is not so. The difficulty only arises when odd-numbered rings are present and one ring is interposed between two others, but it must be emphasised that the nature of the cross-links, and not the odd or even number of the rings, is the important property.

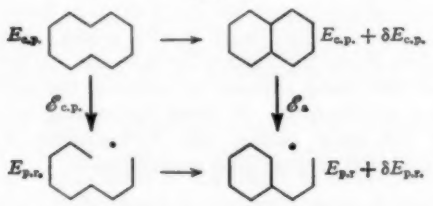
*Method.*—Considering free-radical reactivity first, we require the difference between the total electron energy of the ground state and that of the transition state. Making the usual assumption that the only part of the total electron energy which varies with the structure of the hydrocarbon is the $\pi$-electron energy, we require the difference between the $\pi$-electron energy of the ground and the transition state. It is advantageous if this can be estimated directly, as in Dewar's method,[7] but for the non-alternant hydrocarbons it is necessary to obtain the $\pi$ energies individually. The $\pi$ energy of the ground state is obtained by Dewar and Pettit's cyclic-polyene method,[12] the aromatic hydrocarbon being formally obtained from the corresponding cyclic polyene by the formation of cross-links. The $\pi$ energy of the ground state is then that of the cyclic polyene ($E_{\text{c.p.}}$) plus the change in energy on cross-linking ($\delta E_{\text{c.p.}}$). The $\pi$ energy of the transition state is obtained by extending the method used in the preceding paper to polyene radicals, the latter being cross-linked to build up this state. The $\pi$ energy of the transition state is then that of the linear polyene radical ($E_{\text{p.r.}}$) plus the energy change on cross-linking ($\delta E_{\text{p.r.}}$). The atom localisation energy ($\mathscr{E}_{\text{a}}$) * of the cross-linked hydrocarbon is then

$$\mathscr{E}_{\text{a}} = E_{\text{c.p.}} + \delta E_{\text{c.p.}} - E_{\text{p.r.}} - \delta E_{\text{p.r.}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\mathscr{E}_{\text{a}} = \mathscr{E}_{\text{c.p.}} + \delta E_{\text{c.p.}} - \delta E_{\text{p.r}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $\mathscr{E}_{\text{c.p.}}$ is the atom localisation energy of the cyclic polyene. Equations (1) and (2) can be illustrated diagrammatically, position 1 of naphthalene being used as an example, as in Fig. 1. Ionic localisation energies follow simply from this treatment and bond localisation energies are obtained analogously. The three terms on the right-hand side of eqn. (2) are now calculated in turn.

FIG. 1.




(*a*) *The change in $\pi$-electron energy of a cyclic polyene on cross-linking.* The energy ($e_j$) of the $j$th molecular-orbital ($\psi_j$) of a cyclic polyene ($C_nH_n$) is given,[1] in the usual Hückel approximation, by

$$e_j = 2\beta \cos (2j\pi/n) \ldots . j = 0, \pm 1, \pm 2, \ldots . + n/2 \quad . \quad . \quad . \quad (3)$$

The Coulomb integral of a normal carbon atom is taken as zero, thus fixing the energy zero.† Overlap is neglected and $\beta$ is the standard carbon–carbon bond resonance integral.

* As defined here, $\mathscr{E}$ is a negative energy quantity—a positive numeric times $\beta$, itself a negative energy quantity.

† The sign convention used here is the opposite of that used by Hückel [1] and by Dewar and Pettit [12] and conforms to that used by Coulson and Longuet-Higgins.[25]

[12] Dewar and Pettit, *J.*, 1954, 1617.

The molecular orbitals occur in degenerate pairs, except for the lowest bonding and the highest antibonding, which are not degenerate. The real molecular orbitals are given [1,12,13] by

$$\psi_j\,(\cos) = \sum_{a=1}^{n} \chi_j \cos\,[(2aj\pi/n) + \varepsilon_j]\phi_a$$
$$\psi_j\,(\sin) = \sum_{a=1}^{n} \chi_j \sin\,[(2aj\pi/n) + \varepsilon_j]\phi_a \quad \ldots\ldots (4)$$

where $\chi$, a normalising factor, is $(1/n)^{1/2}$ for the non-degenerate orbitals and $(2/n)^{1/2}$ for the doubly degenerate. The $\phi$'s are carbon $2p$ atomic orbitals and $\varepsilon_j$ is a phase factor.* In favourable cases, correct choice of numbering will cause the phase factor to vanish.

Now Dewar and Pettit show [12] that the formation of a cross-link between atoms $r$ and $s$ of a cylic polyene results in a change $(\delta\varepsilon_j)$ in the energy of the $j$th molecular orbital of

$$\delta\varepsilon_j\,(\cos) = \chi_j^2\beta\{\cos\,[2j(r-s)\pi/n] + \cos\,[(2j(r+s)\pi/n) + 2\varepsilon_j]\}$$
$$\delta\varepsilon_j\,(\sin) = \chi_j^2\beta\{\cos\,[2j(r-s)\pi/n] - \cos\,[(2j(r+s)\pi/n) + 2\varepsilon_j]\} \quad \ldots (5)$$

The resulting change in the total $\pi$-electron energy $(\delta E_{\text{c.p.}})$ † of the cyclic polyene depends on the value of $n$, $(4\gamma + 2)$ or $(4\gamma)$, $\gamma$ being a positive integer.

(1) When $n = (4\gamma + 2)$, *e.g.*, naphthalene or azulene, the cyclic polyene has no non-bonding molecular orbitals and summation of (5) gives

$$\delta E_{\text{c.p.}}\,(4\gamma + 2) = \frac{4\beta}{n} + \frac{8\beta}{n}\sum_{j=1}^{\gamma} \cos\,[2j(r-s)\pi/n] \quad \ldots\ldots (6)$$

The factor of $4\beta/n$ appearing in eqn. (6) is from the lowest bonding molecular orbital, whose phase factor is zero. Summing, we have

$$\delta E_{\text{c.p.}}\,(4\gamma + 2) = \frac{4\beta}{n}\left\{\frac{\sin\,[(r-s)\pi/2]}{\sin\,[(r-s)\pi/n]}\right\} \quad \ldots\ldots (7)$$

and since first-order perturbations are additive, the effect of several cross-links is given by

$$\delta E_{\text{c.p.}}\,(4\gamma + 2) = \frac{4\beta}{n}\sum_{\text{cross}}^{\text{links}}\left\{\frac{\sin\,[(r-s)\pi/2]}{\sin\,[(r-s)\pi/n]}\right\} \quad \ldots\ldots (8)$$

When atoms of like parity are linked, $(r-s)/2$ is an integer and $\delta E_{\text{c.p.}}(4\gamma + 2)$ is zero. The $\pi$-electron energy of a $(4\gamma + 2)$ cyclic polyene is thus unchanged when cross-links are formed between atoms of like parity, while the effect of cross-linking atoms of opposite parity is given by eqn. (8).

(2) When $n = (4\gamma)$, *e.g.*, pentalene or heptalene, the cyclic polyene has two non-bonding molecular orbitals containing two electrons. These orbitals being omitted for the moment, the change in the $\pi$-electron energy $[\delta E_{\text{c.p.}}'(4\gamma)]$ on cross-linking is

$$\delta E_{\text{c.p.}}'(4\gamma) = \frac{4\beta}{n} + \frac{8\beta}{n}\sum_{j=1}^{\gamma-1}\{\cos\,[2(r-s)j\pi/n]\} \quad \ldots\ldots (9)$$

$$= \frac{4\beta}{n}\left\{\sin\left[(r-s)\frac{\pi}{2}\right]\cot\left[(r-s)\frac{\pi}{n}\right] - \cos\left[(r-s)\frac{\pi}{2}\right]\right\} \quad (10)$$

* The phase factor is fully discussed by Dewar and Pettit.[12] It is given by

$$\tan(2\varepsilon_j) = -\sum_{\text{cross}}^{\text{links}} \sin\,[2j(r+s)\pi/n] \Big/ \left(\sum_{\text{cross}}^{\text{links}} \cos.[2j(r+s)\pi/n]\right),$$ $r$ and $s$ being the cross-linked atoms.

† Unless the contrary is stated, throughout this paper we deal with the total $\pi$-electron energy, not with the total energy of the occupied M.O.s.

[13] Moffitt, *J. Chem. Phys.*, 1954, **22**, 323.

When atoms of like parity are linked, $(r - s)/2$ is an integer and the first term in the braces vanishes. When several cross-links are formed

$$\delta E_{\text{c.p.}}'(4\gamma) = \frac{4\beta}{n} \sum_{\text{cross}}^{\text{links}} \left\{ \sin\left[(r-s)\frac{\pi}{2}\right] \cot\left[(r-s)\frac{\pi}{n}\right] - \cos\left[(r-s)\frac{\pi}{2}\right] \right\} \quad . \quad (11)$$

The change in the $\pi$ energy of the cosine wave function non-bonding molecular orbital $[\delta\epsilon_{\text{c.p.}}^{\circ}\ (\cos)]$ is *

$$\delta\epsilon_{\text{c.p.}}^{\circ}\ (\cos) = \frac{2\beta}{n} \left\{ \cos\left[(r-s)\frac{\pi}{2}\right] + \cos\left[(r+s)\frac{\pi}{2} + 2\epsilon^{\circ}\right] \right\} \quad . \quad . \quad (12)$$

and for several cross-links

$$\delta\epsilon_{\text{c.p.}}^{\circ}\ (\cos) = \frac{2\beta}{n} \sum_{\text{cross}}^{\text{links}} \left\{ \cos\left[(r-s)\frac{\pi}{2}\right] + \cos\left[(r+s)\frac{\pi}{2} + 2\epsilon^{\circ}\right] \right\} \quad . \quad . \quad (13)$$

Similarly, for the sine wave function non-bonding molecular orbital

$$\delta\epsilon_{\text{c.p.}}^{\circ}\ (\sin) = \frac{2\beta}{n} \sum_{\text{cross}}^{\text{links}} \left\{ \cos(r-s)\frac{\pi}{2} - \cos\left[(r+s)\frac{\pi}{2} + 2\epsilon^{\circ}\right] \right\} \quad . \quad . \quad (14)$$

The pair of electrons which originally occupied the non-bonding molecular orbitals now inhabit whichever of the perturbed non-bonding molecular orbitals is of lower energy. The total change in the $\pi$-electron energy of the $(4\gamma)$ cyclic polyene $[\delta E_{\text{c.p.}}(4\gamma)]$ on the formation of several cross-links is found by eqns. (11) and (13) or (14) to be

$$\delta E_{\text{c.p.}}(4\gamma) = \frac{4\beta}{n} \left\{ \sum_{\text{cross}}^{\text{links}} \sin(r-s)\frac{\pi}{2} \cos(r-s)\frac{\pi}{n} \pm \sum_{\text{cross}}^{\text{links}} \cos\left[(r+s)\frac{\pi}{2} + 2\epsilon^{\circ}\right] \right\} \quad (15)$$

the plus sign being taken when the perturbed non-bonding molecular orbital having a cosine wave function is of lower energy and the minus sign if the reverse is the case.

(*b*) ***The change in the $\pi$-electron energy of a linear polyene radical on cross-linking.*** In the preceding paper, the effect of the formation of cross-links on the $\pi$-electron energy of a linear polyene was examined. Now the energy and wave functions of the polyene radical molecular orbitals are given by the same formulæ as are those of a linear polyene [14] but the presence of the singly-occupied non-bonding molecular orbital prevents the immediate carrying over of the polyene results to the polyene radical. For this reason, and also because the behaviour of the non-bonding molecular orbital on cross-linking determines the ionic reactivity, this molecular orbital is treated separately from the remaining bonding orbitals.

Consider a polyene radical $(C_{n-1}H_{n+1})$. The change in the $\pi$ energy $(\delta E_{\text{p.r.}}')$ of the electrons of the bonding, doubly-occupied molecular orbitals on cross-linking atoms $r$ and $s$ follows in a similar manner to eqn. (9) of the preceding paper

$$\delta E_{\text{p.r.}}' = \frac{2\beta}{n} \left\{ \frac{\sin[(r-s)(n-1)\pi/2n]}{\sin[(r-s)\pi/2n]} - \frac{\sin[(r+s)(n-1)\pi/2n]}{\sin[(r+s)\pi/2n]} \right\} \quad . \quad (16)$$

Expanding the $(n - 1)$ terms of the numerators, we have

$$\delta E_{\text{p.r.}}' = \frac{2\beta}{n} \left\{ \sin[(r-s)\pi/2] \cot[(r-s)\pi/2n] - \sin[(r+s)\pi/2] \cot[(r+s)\pi/2n] \right\}$$
$$- \frac{2\beta}{n} \left\{ \cos[(r-s)\pi/2] - \cos[(r+s)\pi/2] \right\} \quad . \quad . \quad (17)$$

* $\epsilon^{\circ}$ is the phase factor for the non-bonding molecular orbitals.

[14] Coulson, *Proc. Roy. Soc.*, 1938, *A*, **164**, 393.

Now consider the change in the π energy ($\delta e_{p.r.}^{\circ}$) of the non-bonding molecular orbital. From eqn. (4) of the preceding paper, it is given by

$$\delta e_{p.r.}^{\circ} = \frac{4\beta}{n} \sin (rj\pi/n) \,.\, \sin (sj\pi/n) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (18)$$

and since $j = n/2$ for this orbital

$$\delta e_{p.r.}^{\circ} = \frac{2\beta}{n} \Big\{ \cos [(r - s)\pi/2] - \cos [(r + s)\pi/2] \Big\} \quad . \quad . \quad . \quad . \quad (19)$$

Hence the total change in the π energy of a linear polyene on cross-linking atoms $r$ and $s$ is

$$\delta E_{p.r.} = (2\beta/n) \{ \sin [(r - s)\pi/2] \cot [(r - s)\pi/2n] - \sin [(r + s)\pi/2] \cot [(r + s)\pi/2n] \} \quad (20)$$

When atoms of like parity are linked, both $(r - s)/2$ and $(r + s)/2$ are integers, both terms in the braces in eqn. (20) vanish and there is no change in the total π-electron energy of a linear polyene radical on the formation of such cross-links. There is, however, a change in the energy of the non-bonding molecular orbital. When atoms of opposite parity are cross-linked, there is a change in the total π-electron energy, but there is no change in the energy of the non-bonding molecular orbital. These results are in agreement with those of the exact method. The formation of several cross-links is dealt with in the usual way, eqn. (20) being summed over the cross-links.

(*c*) *The atom localisation energies of a cyclic polyene.* These are easily found. The π-electron energy ($E_{c.p.}$) of a cyclic polyene ($C_nH_n$) depends on the value of $n$, $(4\gamma + 2)$, or $(4\gamma)$.

$$E_{c.p.}(4\gamma + 2) = 4\beta + 8\beta \sum_{j=1}^{\gamma} \cos (2j\pi/n) \quad . \quad . \quad . \quad . \quad . \quad (21)$$

$$= 4\beta \operatorname{cosec} (\pi/n) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (22)$$

and

$$E_{c.p.}(4\gamma) = 4\beta + 8\beta \sum_{j=1}^{\gamma-1} \cos (2j\pi/n) \,. \quad . \quad . \quad . \quad . \quad (23)$$

$$= 4\beta \cot (\pi/n) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (24)$$

The transition state is a polyene radical, whose π-electron energy is

$$E_{p.r.} = 4\beta \sum_{j=1}^{(n/2)-1} \cos (j\pi/n) \quad . \quad . \quad . \quad . \quad . \quad . \quad (25)$$

$$= 2\beta [\cot (\pi/2n) - 1] \quad . \quad . \quad . \quad . \quad . \quad . \quad (26)$$

The atom localisation energies ($\mathscr{E}$) for free radical substitution are then

$$\mathscr{E}_{c.p.}(4\gamma + 2) = 4\beta \operatorname{cosec} (\pi/n) - 2\beta \cot (\pi/2n) + 2\beta \quad . \quad . \quad . \quad (27)$$

$$\mathscr{E}_{c.p.}(4\gamma) = 4\beta \cot (\pi/n) - 2\beta \cot (\pi/2n) + 2\beta \quad . \quad . \quad . \quad . \quad (28)$$

After some manipulation, these reduce to

$$\mathscr{E}_{c.p.}(4\gamma + 2) = 2\beta[1 + \tan (\pi/2n)] \quad . \quad . \quad . \quad . \quad . \quad (29)$$

$$\mathscr{E}_{c.p.}(4\gamma) = 2\beta[1 - \tan (\pi/2n)] \quad . \quad . \quad . \quad . \quad . \quad (30)$$

This completes the evaluation of the three terms on the right-hand side of eqn. (2) and we can now obtain the atom localisation energies for free radical substitution for all of the

purely cyclic alternant and non-alternant hydrocarbons. Collecting these terms together, we have

$$\mathscr{E}_a(4\gamma+2) = 2\beta[1+\tan(\pi/2n)] + \frac{4\beta}{n}\left\{\sum_{\text{cross}}^{\text{links}} \frac{\sin[(r-s)\pi/2]}{\sin[(r-s)\pi/n]}\right\}$$
$$-\frac{2\beta}{n}\left\{\sum_{\text{cross}}^{\text{links}} \sin[(r-s)\pi/2]\cot[(r-s)\pi/2n] - \sin[(r+s)\pi/2]\cot[(r+s)\pi/2n]\right\} \quad (31)$$

$$\mathscr{E}_a(4\gamma) = 2\beta[1-\tan(\pi/2n)] +$$
$$\frac{4\beta}{n}\left\{\sum_{\text{cross}}^{\text{links}} \sin\left[(r-s)\frac{\pi}{2}\right]\cot\left[(r-s)\frac{\pi}{n}\right] \pm \sum_{\text{cross}}^{\text{links}} \cos\left[(r+s)\frac{\pi}{2}+2\epsilon^\circ\right]\right\}$$
$$-\frac{2\beta}{n}\left(\sum_{\text{cross}}^{\text{links}}\left\{\sin\left[(r-s)\frac{\pi}{2}\right]\cot\left[(r-s)\frac{\pi}{2n}\right] - \sin\left[(r+s)\frac{\pi}{2}\right]\cot\left[(r+s)\frac{\pi}{2n}\right]\right\}\right) \quad (32)$$

In eqns. (31) and (32), the first summation(s) on the right-hand side refers to the ground state, the second to the cross-linked radical of the transition state.

The free-radical localisation energies calculated from eqns. (31) and (32) are reported in Tables 1, 2, and 3, together with those obtained by solution of the secular equations [$\mathscr{E}_a$(s.e.)]. In the evaluation of these equations, it often turns out that the non-alternant hydrocarbons are more easily calculated than are the alternants.

TABLE 1. *Atom localisation energies of alternant hydrocarbons.*

| Hydrocarbon | Position | Localisation energy (units of $\beta$) $\mathscr{E}_a$ | $\mathscr{E}_a$(s.e.) [16] |
|---|---|---|---|
| Benzene (a) | — | 2·54 | 2·54 |
| Naphthalene (b) | 1 | 2·42 | 2·30 |
| | 2 | 2·55 | 2·48 |
| Anthracene (c) | 1 | 2·44 | 2·25 |
| | 2 | 2·57 | 2·40 |
| | 9 | 2·12 | 2·01 |
| Phenanthrene (d) | 1 | 2·51 | 2·30 |
| | 2 | 2·57 | 2·50 |
| | 3 | 2·51 | 2·41 |
| | 4 | 2·58 | 2·39 |
| | 9 | 2·33 | 2·30 |
| Naphthacene (e) | 5 | 2·07 | 1·93 |

TABLE 2. *Atom localisation energies of non-alternant hydrocarbons (units of* $\beta$).

| | | Localisation energy [6] | | | | | |
|---|---|---|---|---|---|---|---|
| | | Radical | | Nucleophilic | | Electrophilic | |
| Hydrocarbon | Position | $\mathscr{E}_a$ | $\mathscr{E}_a$(s.e.) | $\mathscr{E}_a$ | $\mathscr{E}_a$(s.e.) | $\mathscr{E}_a$ | $\mathscr{E}_a$(s.e.) |
| Pentalene (f) | 1 | 2·10 | 1·96 | 1·60 | 1·54 | 2·60 | 2·38 |
| | 2 | 2·10 | 2·03 | 2·10 | 2·03 | 2·10 | 2·03 |
| Azulene (g) * | 1 | 2·32 | 2·26 | 2·72 | 2·60 | 1·92 | 1·92 |
| | 2 | 2·32 | 2·36 | 2·32 | 2·36 | 2·32 | 2·36 |
| | 4 | 2·32 | 2·24 | 1·92 | 1·93 | 2·72 | 2·55 |
| | 5 | 2·32 | 2·34 | 2·32 | 2·34 | 2·32 | 2·34 |
| | 6 | 2·32 | 2·36 | 1·92 | 1·99 | 2·72 | 2·73 |
| Heptalene (h) | 1 | 2·07 | 1·93 | 2·40 | 2·19 | 1·74 | 1·66 |
| | 2 | 2·07 | 2·03 | 2·07 | 2·03 | 2·07 | 2·03 |
| | 3 | 2·07 | 2·03 | 2·40 | 2·36 | 1·74 | 1·71 |

* The azulene figures [$\mathscr{E}_a$(s.e.)] were personally communicated by Dr. R. D. Brown.

*Ionic Substitution.*—In proposing a model for the transition state of ionic substitution, Wheland assumed [6] that the molecular orbitals of the residual molecule * are occupied by one more (nucleophilic) or by one less (electrophilic) electron than in free-radical

* The residual molecule is the parent hydrocarbon with the carbon atom undergoing substitution removed.

TABLE 3. *Atom localisation energies* [$\mathscr{E}_a$(s.e.) *followed by* $\mathscr{E}_a$] *of benzannelated azulenes (units of* β) *for radical, electrophilic, and nucleophilic substitution.*

1 : 2-Benzazulene (i)

| Position | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Radical ..... | 1·53 | 2·17 | 1·39 | 2·27 | — | 2·33 | 1·50 | 2·33 | 1·40 | 2·27 | 1·56 | 2·40 |
| Electro ..... | 1·14 | 1·89 | 1·56 | 2·55 | — | 2·33 | 1·72 | 2·62 | 1·40 | 2·27 | 1·83 | 2·69 |
| Nucleo ..... | 1·93 | 2·46 | 1·22 | 1·98 | — | 2·33 | 1·29 | 2·05 | 1·40 | 2·27 | 1·28 | 2·12 |

4 : 5-Benzazulene (j)

| | 1 | | 2 | | 3 | | 6 | | 7 | | 8 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Radical ..... | 1·54 | 2·33 | — | 2·27 | 1·63 | 2·40 | 1·39 | 2·17 | 1·72 | 2·40 | 1·38 | 2·27 |
| Electro ..... | 1·35 | 2·05 | — | 2·27 | 1·39 | 2·12 | 1·74 | 2·46 | 1·72 | 2·40 | 1·75 | 2·55 |
| Nucleo ..... | 1·74 | 2·62 | — | 2·27 | 1·87 | 2·69 | 1·03 | 1·89 | 1·72 | 2·40 | 1·01 | 1·98 |

5 : 6-Benzazulene (k)

| | 1 | | 2 | | 3 | | 4 | | 7 | | 8 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Radical ..... | 1·60 | 2·33 | 1·70 | 2·33 | 1·52 | 2·27 | 1·34 | 2·17 | 1·48 | 2·17 | 1·50 | 2·40 |
| Electro ..... | 1·36 | 2·05 | 1·70 | 2·33 | 1·33 | 1·98 | 1·65 | 2·46 | 1·48 | 2·17 | 1·64 | 2·69 |
| Nucleo ..... | 1·83 | 2·62 | 1·70 | 2·33 | 1·71 | 2·55 | 1·04 | 1·89 | 1·48 | 2·17 | 1·36 | 2·12 |

$\mathscr{E}_a$(s.e.) are taken from ref. 15 and include overlap, while $\mathscr{E}_a$ neglect overlap.
The sign convention for ionic reactivity used in ref. 15 is the opposite of that used here.

substitution. With this assumption, consider the effect on the terms in eqn. (2) on changing from free-radical to ionic substitution. Clearly, $E_{c.p.}$, $E_{p.r.}$, and $\delta E_{c.p.}$ are unchanged and $\delta E_{p.r.}$ is also unchanged if the non-bonding molecular orbital of the polyene radical is unchanged in energy on cross-linking, *i.e.*, if alternant rings are formed [eqn. (19)]. This conclusion agrees with that from the exact method. If non-alternant rings are formed, this orbital may be changed in energy and the total π-electron energy of the transition state may be affected by the number of electrons occupying this orbital. This result brings out clearly the underlying reason for the difference in ionic reactivity between alternant and non-alternant hydrocarbons.

We need consider, then, only cross-links between atoms of like parity and we require the change in energy of the non-bonding molecular orbital of the polyene radical on cross-linking. This can now be written [eqn. (19)]

$$\delta\epsilon_{p.r.}^{\circ} = \frac{2\beta}{n}[(-1)^{(r-s)/2} - (-1)^{(r+s)/2}] \quad . \quad . \quad . \quad . \quad . \quad (33)$$

If more than one cross-link is formed, eqn. (33) is summed over these cross-links in the usual way. Hence

$$\mathscr{E}_a^- = \mathscr{E}_a - \delta\epsilon_{p.r.}^{\circ} = \mathscr{E}_a - \frac{2\beta}{n}\sum_{cross}^{links}[(-1)^{(r-s)/2} - (-1)^{(r+s)/2}] \quad . \quad . \quad . \quad (34)$$

$$\mathscr{E}_a^+ = \mathscr{E}_a + \delta\epsilon_{p.r.}^{\circ} = \mathscr{E}_a + \frac{2\beta}{n}\sum_{cross}^{links}[(-1)^{(r-s)/2} - (-1)^{(r+s)/2}] \quad . \quad . \quad . \quad (35)$$

where $\mathscr{E}_a^-$ and $\mathscr{E}_a^+$ are the atom localisation energies for nucleophilic and electrophilic substitution respectively. Using equations (34) and (35), we have calculated the ionic localisation energies of some cyclic non-alternant hydrocarbons (Tables 2 and 3).

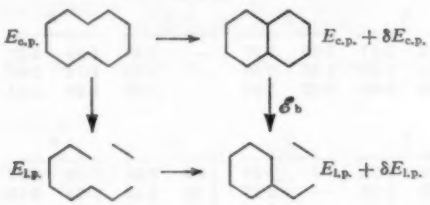
*Bond Localisation Energies.*—In this reaction, the transition state is a polyene, cross-linked at one or more points. The π-electron energy of the ground state of a cyclic polyene and the change in energy have been given [eqns. (8), (15), (22), (24)]. The π-electron energy of a linear polyene and the change in energy on cross-linking have been given in the preceding paper [eqns. (9) and (11)]. From these equations, the bond localisation energies ($\mathscr{E}_b$) of the cross-linked hydrocarbons are

$$\mathscr{E}_b(4\gamma + 2) = 4\beta \text{ cosec } (\pi/n) - 2\beta \text{ cosec } [\pi/2(n-1)] + \delta E_{c.p.} - \delta E_{l.p.} \quad . \quad . \quad (36)$$

$$\mathscr{E}_b(4\gamma) = 4\beta \cot (\pi/n) - 2\beta \text{ cosec } [\pi/2(n-1)] + \delta E_{c.p.} - \delta E_{l.p.} \quad . \quad . \quad . \quad (37)$$

These equations can be illustrated, the 1 : 2-bond of naphthalene being used as an example, as in Fig. 2.

FIG. 2.



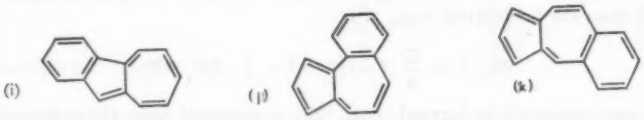

In Table 4, the perturbation ($\mathscr{E}_b$) and secular equation [$\mathscr{E}_b$ (s.e.)] bond localisation energies for the simple non-alternant hydrocarbons are reported.

TABLE 4. *Bond localisation energies for the simple cylic non-alternant hydrocarbons (units of* β).

| Hydrocarbon | Pentalene | | Heptalene | | | Azulene | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Bond | 1 : 2 | 1 : 7 | 1 : 2 | 2 : 3 | 1 : 11 | 1 : 2 | 4 : 5 | 5 : 6 | 1 : 9 | 8 : 9 |
| $\mathscr{E}_b$(s.e.) | 0·99 | 1·47 | 1·04 | 1·14 | 1·56 | 1·37 | 1·31 | 1·42 | 1·85 | 1·85 |
| $\mathscr{E}_b$ | 1·17 | 1·17 | 1·20 | 1·20 | 1·20 | 1·43 | 1·43 | 1·43 | 1·43 | 1·43 |

$\mathscr{E}_b$(s.e.) for pentalene and heptalene are taken from ref. 6. The azulene figures were obtained from published data [9] on the residual molecule or calculated.

An excellent opportunity of testing the perturbation method on more complex non-alternant hydrocarbons is available form the work of Simon, Naville, Susler, and Heilbronner.[15] These workers, in attempting to correlate the observed basicities of azulene and the benzannelated azulenes, have reported free-radical and ionic localisation energies for most positions in 1 : 2-, 4 : 5-, and 5 : 6-benzazulene (i, j, and k respectively). The perturbation method has been applied to these compounds and both sets of results are reported in Table 3.




## DISCUSSION

The perturbation method is first tested on the alternant benzenoid hydrocarbons in Table 1. The perturbation localisation energies reproduce those obtained by solution of the secular equations with satisfactory accuracy and if the perturbation figures are reduced by 0·1β, the agreement is good.

Now consider the atom localisation energies for free-radical substitution in the simple cyclic non-alternant hydrocarbons (Table 2). A particularly simple situation arises when $n$ is $(4\gamma + 2)$, the atom localisation energies for free-radical substitution being those of the corresponding cyclic polyene. Since the localisation energies of the latter hydrocarbons lie in the range 2·32β ($n = 10$) to 2·0β ($n = \infty$), this is also the range of the localisation energies for free-radical reaction of the cross-linked hydrocarbons.

Turning to the specific calculations in Table 2, we find that the agreement between the perturbation localisation energies and those from the secular equations is clear. One shortcoming of the perturbation results is the prediction that all positions in any one simple cyclic non-alternant hydrocarbon are of equal free-radical reactivity. This is an oversimplification but, compared with the very large range of ionic localisation energies, the free-radical localisation energies of these hydrocarbons do approximate to this result.

[15] Simon, Naville, Susler, and Heilbronner, *Helv. Chim. Acta*, 1956, **39**, 1107.

It will be most interesting to discover whether the differences, predicted by the Hückel theory, in the free-radical reactivity of the various positions in, say, azulene are borne out in practice as the self-consistency of the method is lost in non-alternant hydrocarbons.[2e,17]

*Ionic Reactivity.*—It is in this type of reactivity that there is a clear distinction between the alternant and the non-alternant hydrocarbons, the non-alternant ones having an extremely large range of ionic localisation energies. Dewar and his co-workers [11] found a rate variation for nitration of the benzenoid hydrocarbons which would lead to rate differences of the order of $10^{15}$ for some of the non-alternant hydrocarbons discussed in this paper. Only experiment can decide whether changes of mechanism will accompany such large rate differences.

Assuming for the moment that no mechanistic changes occur, we can speculate on the effect of such differences on the chemical properties of these hydrocarbons. From general experience, an electrophilic localisation energy of 2·0β (*e.g.*, anthracene) is sufficiently high for the hydrocarbon to be quite stable under ordinary acidic conditions.[18] By " ordinary conditions " is meant, for example, those of acid-catalysed elimination of HX in the formation of a double bond. When the electrophilic localisation energy falls to 1·9β (*e.g.*, azulene and the benzannelated azulenes [15]), the hydrocarbon is detectably basic. In heptalene, the electrophilic localisation energy of 1·6—1·7β is perhaps sufficiently low for the hydrocarbon to undergo cationic polymerisation during the synthetic operation mentioned above. Preparation of this hydrocarbon would then best be attempted in the absence of strong acids.

There is less information to guide us in considering the allowable limits of nucleophilic localisation energies. The common benzenoid hydrocarbons (nucleophilic localisation energies of greater than 2·0β) are quite stable to the common bases. In pentalene, however, the localisation energy for nucleophilic attack in the 1 position is 1·6β and this may be sufficiently low for anionic polymerisation to occur fairly easily. The preparation of this hydrocarbon would then best be attempted in the absence of strong base.

Such considerations as have been put forward in the last paragraphs are necessarily vague at present, there being little relevant experimentation to guide them. The details of reaction conditions will be of major importance, but where there is a free choice of using either acidic or basic reaction conditions, the uncertainty as to the stability of the product can be reduced by an examination of the theoretical predictions.

The results obtained from the benzazulenes (Table 3) are particularly encouraging, the agreement between the results of the perturbation method and those from the solution of the secular equations being excellent. The disparity in absolute magnitude is due to overlap's being neglected in the perturbation calculations while it is included in the reported results.[15] Clearly the perturbation method picks out the position of protonation as accurately as does the exact method, and there is also good agreement with regard to nucleophilic localisation energies. As with the simple non-alternant hydrocarbons, there is not complete agreement in the radical localisation energies but the differences are small.

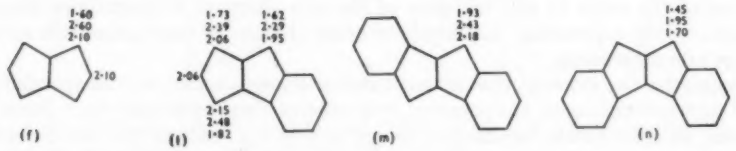
*Bond Localisation Energies.*—The bond localisation energies calculated by the perturbation method are in reasonable agreement with those obtained by solution of the secular equations (Table 4). In particular, the higher bond localisation energy of azulene than pentalene and heptalene is brought out well. Bonds having a carbon atom common to two rings have much higher secular-equation localisation energies than those calculated by the perturbation method, but as such bonds are the least reactive in the molecule, inability to deal with them is not important for studies of chemical reactivity. The remaining bonds in any one simple cyclic non-alternant hydrocarbon are predicted to be of the same localisation energy and, from the exact calculations, this is a reasonable approximation.

[16] Burkitt, Coulson, and Longuet-Higgins, *Trans. Faraday Soc.*, 1951, **47**, 553.
[17] Coulson and Dewar, *Discuss. Faraday Soc.*, 1947, **2**, 54.
[18] Gold and Tye, *J.*, 1952, 2172.

XUM

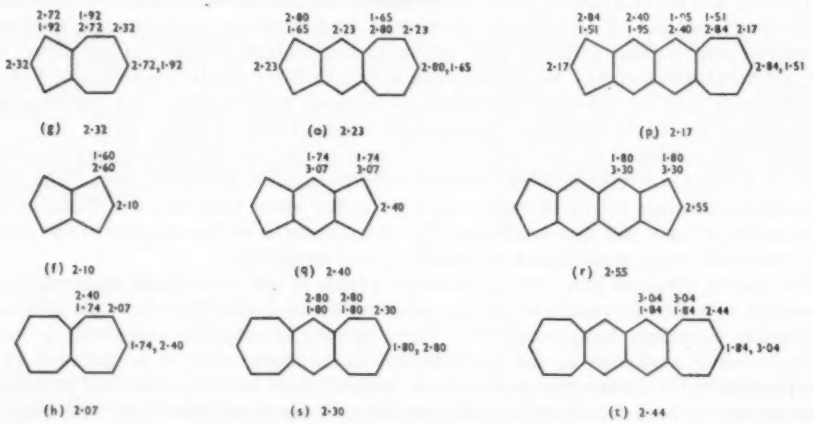
To illustrate the use of the perturbation method, the effect of benzannelation and benzinterposition on the free-radical and ionic reactivity of azulene, pentalene and, in part, heptalene has been examined. The monobenzazulenes have already been dealt with in Table 3; the predicted chemical reactivity of the benzannelated pentalenes is shown in Fig. 3, where the numerals represent, in order from the ring outward, radical, electrophilic, and nucleophilic reactivity.

FIG. 3.




Dibenzopentalene (m) is of particular interest as experimental data are available for it and, at the same time, the same workers using similar synthetic methods were unable to obtain pentalene itself.[19] The theoretical predictions are that monobenzannelation has little effect on the reactivity and that dibenzannelation [in the sense of (m)] has little effect on the free-radical reactivity but does decrease the nucleophilic reactivity substantially. Possibly this reduction in reactivity towards bases is

FIG. 4.




sufficient to allow the benzannelated compound to be isolated, while the simple hydrocarbon is too reactive in this respect. It would also be predicted from the theory that the dibenzopentalene (m) is not basic * and this agrees with the experimental observation that it does not dissolve in orthophosphoric acid, in which azulene and the benzannelated azulenes are soluble. The observation [19] that dibenzopentalene (m) is destroyed by concentrated sulphuric acid and is polymerised by concentrated hydrochloric acid suggests that these two acids are not acting as simple protonating media, but have other modes of chemical reactivity here. In fact, the situation suggests an interesting possibility which could arise with some of the non-alternant hydrocarbons. Consider a hydrocarbon which has little reactivity towards electrophils, but is reactive towards bases. It then becomes possible for reaction with, say, hydrochloric acid to occur by the chlorine anion's attacking

* A position with an electrophilic localisation energy of some 1·9—2·0$\beta$ or lower being assumed to be required for basicity.

[19] Blood and Linstead, *J.*, 1952, 2255, 2263.

first. Such mechanistic variations are to be expected with some non-alternant hydrocarbons. The effect of dibenzannelation of pentalene in the sense of (n) is markedly to increase the free-radical and the ionic reactivity.

The effect of benzinterposition on azulene, pentalene, and heptalene is shown in Fig. 4. The numeral closer to the ring represents electrophilic reactivity, that further out the nucleophilic reactivity. Where they are the same, only one is quoted. The numeral beside the identifying letter is the radical reactivity for all positions.

In azulene, benzinterposition (o) and (p) does not change the predicted orientation of substitution but the free-radical reactivity is increased slightly and the ionic reactivity is increased substantially. When two benzene rings are interposed (p), both the electrophilic and the nucleophilic reactivities are reduced to $1{\cdot}51\beta$ at different positions. Preparation of this hydrocarbon would then best be attempted in the absence of both strong acid and strong base.

In pentalene and heptalene, benzinterposition does not change the predicted orientation of substitution, but now the ionic reactivity is decreased. Both mono- and di-benzinterposed pentalenes should be quite stable to simple protonating media but, as the dibenzopentalene data [19] show, caution is required in assuming that the common mineral acids do not react in other ways with these very reactive hydrocarbons. Conversely, the mono- and di-benzinterposed heptalenes should be quite stable to bases but should be quite basic.

The author is indebted to Dr. R. D. Brown for the azulene figures (Table 2) and to Professor M. J. S. Dewar for advice.

ROYAL HOLLOWAY COLLEGE, ENGLEFIELD GREEN, SURREY. [*Received, September 27th*, 1957.]

---

## 207. *Structure and Properties of Mesomeric Systems. Part III.* Charge Distribution and Related Properties in Non-alternant Hydrocarbons.*

By DAVID PETERS.

A perturbation method is used to obtain the charge distribution in some of the larger cyclic non-alternant hydrocarbons. Several properties related to charge distribution are discussed.

IN Part II,* perturbation methods were used to study the chemical reactivity of the larger non-alternant hydrocarbons. Atom localisation energies for ionic and free-radical reaction have been obtained in a simple manner, thus eliminating the excessive labour involved in the conventional procedure. We now examine charge distribution in the ground state of mesomeric hydrocarbons, a property which is important in itself and also in several applications. In alternant hydrocarbons, the charge distribution is, in the Hückel approximation, uniform throughout the ring, the charge on each carbon atom being unity.[1] In the non-alternant hydrocarbons, however, there is an uneven charge distribution [1,2,3] but its formal calculation is tedious and a perturbation method by which it may be obtained is now described.

The approach to be adopted follows from the work of Coulson and Longuet-Higgins [4] and of Dewar and Pettit.[5] The former authors have developed a series of polarisabilities, the one of interest here being the atom–bond polarisability $\pi_{t,rs}$:

$$\pi_{t,rs} = \delta q_t/\delta\beta_{rs} = 4\sum_{p=1}^{m}\sum_{q=m+1}^{n}[c_{tp}c_{tq}(c_{rp}c_{rq} + c_{sq}c_{rp})/(\epsilon_p - \epsilon_q)] \quad . \quad . \quad . \quad (1)$$

* Part II, preceding paper.

[1] Coulson and Rushbrooke, *Proc. Camb. Phil. Soc.*, 1940, **36**, 193.
[2] Brown, *Trans. Faraday Soc.*, 1948, **44**, 984; 1949, **45**, 296.
[3] Coulson and Longuet-Higgins, *Rev. Sci.*, 1947, **85**, 929.
[4] Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, *A*, **191**, 39; 1947, *A*, **192**, 16.
[5] Dewar and Pettit, *J.*, 1954, 1617.

This quantity describes the change ($\delta q_t$) in the charge on atom $t$ resulting from a change ($\delta\beta_{rs}$) in the resonance integral of the bond between atoms $r$ and $s$. The bonding molecular orbitals are $1 - m$, the antibonding $(m + 1) - n$; the $c$'s are atomic-orbital coefficients of self-evident nomenclature and $e_q$ and $e_p$ are the energies of the $q$th and $p$th molecular orbitals.

Dewar and Pettit [5] have used the analogous bond–bond polarisability $\pi_{st,uv}$ to estimate the effect on the bond orders of the peripheral bonds of the formation of the cross-links in the benzenoid hydrocarbons.

We wish to know what will be the effect on the charge on the other carbon atoms of the formation of such cross-links. As an example, we regard azulene as being derived from *cyclo*decapentaene by the formation of the cross link (the numbering used is not the usual chemical numbering):

and the polarisability $\pi_{1,6:10}$ will give an estimate of the change in the charge on carbon atom 1 resulting from the formation of the 6 : 10 cross-link. The charge on all carbon atoms of the parent cyclic polyene is, of course, unity.

Now Coulson and Longuet-Higgins show [4] that the degeneracy of all but the highest antibonding and the lowest bonding molecular orbitals of the cyclic polyene necessitates our using the correct zeroth-order wave functions ($\psi$) for the degenerate levels: *

$$\left.\begin{aligned}\psi_j(\cos) &= \chi_j \sum_{a=1}^{n} \cos\left(2aj\frac{\pi}{n} + \varepsilon_j\right)\phi_a \\ \psi_j(\sin) &= \chi_j \sum_{a=1}^{n} \sin\left(2aj\frac{\pi}{n} + \varepsilon_j\right)\phi_a\end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Rather different treatments are required for the $(4\gamma + 2)$ and the $(4\gamma)$ cycles and the former class is dealt with first.

*The* $(4\gamma + 2)$ *Hydrocarbons.*—The nomenclature of eqn. (1) being modified slightly for the cyclic polyenes, the occupied molecular orbitals are $0$—$\gamma$, the unoccupied $(\gamma + 1)$—$(2\gamma + 1)$ and eqn. (1) becomes

$$\pi_{t,rs} = 4\sum_{j=0}^{\gamma} \sum_{k=\gamma+1}^{2\gamma+1} [c_{tj}c_{tk}(c_{sj}c_{rk} + c_{rj}c_{sk})/(e_j - e_k)] \quad . \quad . \quad . \quad . \quad (3)$$

In this equation, the first summation is to be taken over all the bonding, the second over all the antibonding, orbitals and for each value of $j$ and $k$ there are two orbitals having cosine and sine wave functions (2).

Reduction of equation (3) gives (Appendix 1)

$$\pi_{t,rs} = 4\sum_{j=0}^{\gamma} \sum_{k=\gamma+1}^{2\gamma+1} \frac{\chi_j^2 \cdot \chi_k^2}{(e_j - e_k)} \left\{\cos 2(t-r)k\frac{\pi}{n} \cdot \cos 2(t-s)j\frac{\pi}{n} + \cos 2(t-r)j\frac{\pi}{n} \cdot \cos 2(t-s)k\frac{\pi}{n}\right\} \quad . \quad . \quad (4)$$

The disappearance of $\varepsilon$ is a useful result, the practical significance being that the numbering of the cyclic polyene is arbitrary. Further reduction (Appendix 2) gives

$$\pi_{t,rs} = 2\left[\cos(t-r)\pi + \cos(t-s)\pi\right]\left[\sum_{j=0}^{\gamma} \frac{\chi_j^4}{e_j}\left\{\cos 2(t-s)j\frac{\pi}{n} \cdot \cos 2(t-r)j\frac{\pi}{n}\right\} + 2\sum_{j=0}^{\gamma-1} \sum_{h=j+1}^{\gamma} \frac{\chi_j^2 \cdot \chi_h^2}{(e_j + e_h)}\left\{\cos 2(t-r)j\frac{\pi}{n} \cdot \cos 2(t-s)h\frac{\pi}{n} + \cos 2(t-s)j\frac{\pi}{n} \cos 2(t-r)h\frac{\pi}{n}\right\}\right] \quad . \quad . \quad . \quad (5)$$

* The energy levels and the wave functions of a cyclic polyene and the phase factor $\varepsilon$ are described in the preceding paper. Symbols common to both papers are as defined there.

Now the term in the first pair of brackets vanishes when the cosines are +1 and −1 and this occurs when atoms $r$ and $s$ are of opposite parity. Since the cross-linking of such atoms generates alternant hydrocarbons, we have the result, obtained in another way by Coulson and Longuet-Higgins,[4] that $\pi_{t,rs}$ is zero for these hydrocarbons. When cross-links are formed between atoms of like parity, this term is $\pm 2$, the plus sign being taken when $r$ and $s$ belong to the same set as $t$, and the minus sign when they belong to the opposite set to $t$. These results hold when several cross-links are present in the same hydrocarbon, first-order perturbations being additive. The total charge on atom $t$ after the formation of several cross-links is

$$q_t = 1 + \sum_{\text{cross}}^{\text{links}} \pi_{t,rs} \cdot \beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

*The (4γ) Hydrocarbons.*—In these hydrocarbons, the situation is complicated by the presence in the cyclic polyene of the two non-bonding molecular orbitals, each of which contains a single electron. There results a mathematical difficulty which does not invalidate the method completely but does preclude analysis of the general case.

Consider the cross-linked hydrocarbon in which all the degeneracy of the molecular orbitals of the parent cyclic polyene has been removed by the perturbation. The two electrons of the non-bonding molecular orbitals of the cyclic polyene will now inhabit the perturbed non-bonding molecular-orbital of lower energy. The change in energy of these orbitals on cross-linking ($\delta e_{\text{o.p.}}{}^{\circ}$) is given by eqn. (12) of the preceding paper:

$$\delta e_{\text{o.p.}}{}^{\circ} = \frac{2\beta}{n}\left\{\cos (r-s)\frac{\pi}{2} \pm \cos\left[(r+s)\frac{\pi}{2} + 2\varepsilon^{\circ}\right]\right\} \quad . \quad . \quad . \quad . \quad (7)$$

the plus sign being taken for the cosine wave function and the minus sign for the sine wave function.

Equation (1) is applicable to the cross-linked hydrocarbon, the summation nomenclature being modified slightly to give

$$\pi_{t,rs}{}' = 4\sum_{p}^{\text{occ.}} \sum_{q}^{\text{unocc.}} [c_{tp}c_{tq}(c_{rp}c_{rq} + c_{sq}c_{rp})/(e_p - e_q)] \quad . \quad . \quad . \quad . \quad (8)$$

The significance of the prime is discussed shortly. Now consider the effect of removing the perturbation. Following Coulson and Longuet-Higgins,[4] assume that the π-electron energy and its derivatives are continuous functions of the perturbation, then the value of $\pi_{t,rs}{}'$ for the unperturbed molecule will be the limit of $\pi_{t,rs}{}'$ as the perturbation vanishes, if such a limit exists. As this process occurs, the molecular orbitals move towards the degenerate pairs of the cyclic polyene and all terms in eqn. (8) behave normally with one exception—the term in which $p$ and $q$ are the occupied and unoccupied non-bonding molecular orbitals respectively. Writing out this term ($\rho$) in full, we have:

$$\rho = \frac{16\beta}{n}\left[\frac{\cos\left(t\frac{\pi}{2} + \varepsilon^{\circ}\right)\cdot \sin\left(t\frac{\pi}{2} + \varepsilon^{\circ}\right)}{(e_p - e_q)}\right]\left[\cos\left(r\frac{\pi}{2} + \varepsilon^{\circ}\right)\cdot \sin\left(s\frac{\pi}{2} + \varepsilon^{\circ}\right) + \cos\left(s\frac{\pi}{2} + \varepsilon^{\circ}\right)\cdot \sin\left(r\frac{\pi}{2} + \varepsilon^{\circ}\right)\right] \quad . \quad . \quad (9)$$

$$= \frac{8\beta}{n} \sin (t\pi + 2\varepsilon^{\circ}) \cdot \sin\left[(r+s)\frac{\pi}{2} + 2\varepsilon^{\circ}\right]/(e_p - e_q) \quad . \quad . \quad . \quad (10)$$

Now in certain cases—when $\varepsilon^\circ$ is zero, for example—the numerator vanishes for all values of $e_p$ and $e_q$ and so, by assumption, the term is zero when $e_p$ and $e_q$ are zero. When cross-links are formed between atoms of like parity only, $\varepsilon^\circ$ is zero and $\rho$ is zero. When cross-links are formed between atoms of opposite parity only, $(r+s)$ is odd and $2\varepsilon^\circ$ is often $\pm\pi/2$ and $\rho$ vanishes again. The term becomes indeterminate when $\varepsilon^\circ$ assumes an intermediate value. In what follows, it is assumed that $\rho$ is zero but it must be emphasised that the conclusions are only valid when this is the case.

The polarisability $\pi_{t,rs}'$ does not refer to the cyclic polyene itself, in which the non-bonding molecular orbitals are both singly occupied, but to the artificial state in which one of these orbitals is doubly occupied and the other is empty. The charge distribution is not uniform in the latter state and the charge $(\delta q_t^\circ)$ resulting from this electron reorganisation must be added to $\delta q_t'$ to produce the total charge $(q_t)$ of the $t$th carbon atom of the cross-linked hydrocarbon. It is easily shown that

$$\delta q_t^\circ = \pm\frac{2}{n}\left[\cos^2\left(t\frac{\pi}{2}+\varepsilon^\circ\right)-\sin^2\left(t\frac{\pi}{2}+\varepsilon^\circ\right)\right] = \pm\frac{2}{n}\cos\left(t\pi+2\varepsilon^\circ\right) \quad . \quad (11)$$

the plus sign being taken when the cosine wave function is doubly occupied and the minus sign when the sine wave function is doubly occupied. The total charge $(q_t)$ resulting from the formation of one cross-link is give by

$$(q_t-1) = \pi_{t,rs}'\cdot\beta+\delta q_t^\circ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

$$= 4\sum^{\text{occ.}}\sum_{k}^{\text{unocc.}}[c_{rj}c_{tk}(c_{sj}c_{sk}+c_{rj}c_{rk})/(e_j-e_k)]$$

$$\pm\frac{2}{n}\cos\left(t\pi+2\varepsilon^\circ\right) \quad . \quad . \quad (13)$$

and reduction of the first term on the right-hand side of eqn. (13) gives (Appendix 3)

$$(q_t-1) = 2\left[\cos(t-r)\pi+\cos(t-s)\pi\right]\left\{\sum_{j=0}^{\gamma-1}\left[\frac{\chi_j^4}{e_j}\cdot\cos 2(t-s)j\frac{\pi}{n}\cdot\cos 2(t-r)j\frac{\pi}{n}\right]\right.$$

$$\left.+2\sum_{j=0}^{\gamma-2}\sum_{h=j+1}^{\gamma-1}\frac{\chi_j^2\cdot\chi_h^2}{(e_j+e_h)}\left[\cos 2(t-r)j\frac{\pi}{n}\cdot\cos 2(t-s)h\frac{\pi}{n}+\cos 2(t-s)j\frac{\pi}{n}\cos 2(t-r)h\frac{\pi}{n}\right]\right\}$$

$$+4\left[\sin\left(t\frac{\pi}{2}+\varepsilon^\circ\right)\cdot\sin\left(s\frac{\pi}{2}+\varepsilon^\circ\right)+\cos\left(t\frac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos\left(s\frac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos(t-r)\pi\right]\times$$

$$\left[\sum_{j=0}^{\gamma-1}\frac{\chi_y^2\cdot\chi_j^2}{e_j}\cos 2(t-r)j\frac{\pi}{n}\right]$$

$$+4\left[\sin\left(t\frac{\pi}{2}+\varepsilon^\circ\right)\cdot\sin\left(r\frac{\pi}{2}+\varepsilon^\circ\right)+\cos\left(t\frac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos\left(r\frac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos(t-s)\pi\right]\times$$

$$\left[\sum_{j=0}^{\gamma-1}\frac{\chi_y^2\cdot\chi_j^2}{e_j}\cos 2(t-s)j\frac{\pi}{n}\right]$$

$$\pm\frac{2}{n}\cos\left(t\pi+2\varepsilon^\circ\right) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

In eqn. (14), it has been assumed that the cosine wave function non-bonding molecular orbital is doubly occupied and the sine wave function non-bonding molecular orbital is unoccupied. If the converse is the case, the equation must be modified slightly as shown in Appendix (3).

From eqns. (5) and (14) we can calculate the charge distribution of all of the $(4\gamma + 2)$ non-alternant hydrocarbons and of some of the $(4\gamma)$ representatives. Formal calculations of the charge distribution of the simpler non-alternant hydrocarbons have been reported [1,2,3] and these results $[10^3(1 - q_i)]$ are compared (inner numerals) in Fig. 1 with

FIG. 1.

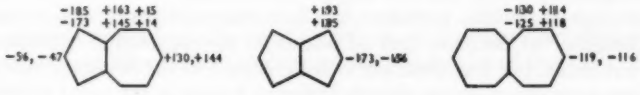
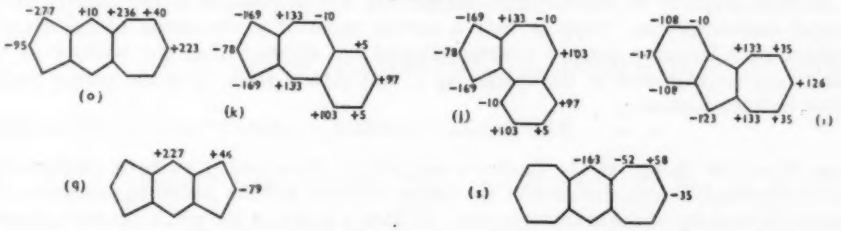



FIG. 2.




the results of the perturbation method (outer numerals). To illustrate the use of the latter technique, the charge distribution of some of the larger non-alternant hydrocarbon has been calculated and the results $[10^3(1 - q_i)]$ are reported in Fig. 2. For convenience, aromatic bonds are omitted.

## DISCUSSION

Comparison of the perturbation charge distribution and the exact figures, where the latter are available (Fig. 1), shows that the perturbation method reproduces the sign and the magnitude of the charges with very encouraging accuracy. A more extensive comparison is precluded by the scarcity of formal calculations and this shortage emphasises the great amount of labour involved in the complete treatment.

Using the perturbation method, we can examine the charge distribution of the larger non-alternant hydrocarbons (Fig. 2). Linear benzinterposition has little effect on the orientation of charge in azulene, pentalene, or heptalene, but the sizes of the charges are substantially altered, those in azulene being increased, those in pentalene and heptalene being reduced. Benzannelation has a relatively small effect on the charge distribution of azulene, both the orientation and the sizes of the charges remaining almost unchanged. The perturbation method is not generally applicable to the benzannelated pentalenes and heptalenes. As is discussed below, there is a good parallel between the charges and the ionic localisation energies of these hydrocarbons.

Charge distribution plays an important part in several properties of mesomeric systems.[7] The most direct result of an uneven charge distribution is the existence, in an unsymmetrical hydrocarbon, of a dipole moment, but in this application, some refinement of the simple Hückel method is required to obtain results of more than qualitative significance (cf. ref. 7, chap. 7). For this reason, the subject is not examined further now.

Charge distribution is fundamental to one of the two molecular-orbital theories of chemical reactivity—the isolated-molecule approximation.[8] In this approach, it is supposed that the carbon atom having the greatest surplus of positive or negative charge in the ground state will be the preferred position of attack by nucleophils and electrophils,

[6] Hückel, *Z. Physik*, 1930, **60**, 423; 1931, **70**, 204; 1931, **72**, 310; 1932, **76**, 628.
[7] Pullman and Pullman, "Les Théories Electroniques de la Chimie Organique," Masson et Cie., Paris, 1952.
[8] R. D. Brown, *Quart. Rev.*, 1952, **6**, 63.

respectively. While this assumption is probably less sound than the localisation method used in the preceding paper, it is interesting to compare the results from both sources. Such comparison shows that there is good qualitative agreement as to the most reactive position for ionic substitution in all of the hydrocarbons studied. This agreement strongly reinforces our confidence in the perturbation methods. For example, both methods predict that benzinterposition will not change the orientation of ionic substitution in the odd-numbered rings of azulene, pentalene and heptalene and that it will increase the ionic reactivity of azulene but decrease that of pentalene and heptalene. Quantitatively, the agreement is not exact, but this situation is not confined to the results of the perturbation method, the two approaches giving slightly different results in the exact treatment for the azulene molecule.

Another property in which charge distribution is of importance is the basicity of the derived azaheterocycle. Suppose that a carbon atom of a mesomeric hydrocarbon is replaced by a nitrogen atom. Longuet-Higgins has shown [9] that the basicity of the azaheterocycles is related to the charge ($q_t$) at this carbon atom ($t$) in the parent hydrocarbon by the equation:

$$2{\cdot}3RT \cdot \mathrm{p}K_a = \text{constant} - q_t\delta\alpha_t \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

where $\delta\alpha_t$ is the change in the Coulomb integral of the nitrogen atom on protonation. Since $\delta\alpha$ is negative here, the greater the charge on atom $t$ of the parent hydrocarbon, the greater the basicity of the azaheterocycle. In fact, a graph of the p$K_a$'s against $q_t$ should give a straight line having a positive slope. Longuet-Higgins shows [9] that this result is approximately true for a number of compounds. Since we can now obtain the charge distribution of many of the larger non-alternant hydrocarbons, it is simple to predict the basicities of the derived azaheterocycles. A few compounds of this type have been reported recently [10] but there seem to be no data by which the perturbation method can be tested.

## Appendix 1

It is required to obtain equation (4) from equation (3). We have

$$\pi_{t,rs} = 4\sum_{j=0}^{\gamma}\sum_{k=\gamma+1}^{2\gamma+1}[c_{tj}c_{tk}(c_{sj}c_{rk} + c_{sk}c_{rj})/(e_j - e_k)] \quad . \quad . \quad . \quad . \quad (3)$$

Consider one bonding pair of degenerate molecular orbitals ($j$) and one antibonding degenerate pair ($k$), the respective phase factors being $\varepsilon_j$ and $\varepsilon_k$. The single term arising from the bonding cosine wave function $[\psi_j(\cos)]$ and the antibonding cosine wave function $[\psi_k(\cos)]$ is

$$4\,\frac{\chi_j^2\cdot\chi_k^2}{(e_j - e_k)}\cos\left(2tj\frac{\pi}{n} + \varepsilon_j\right)\cdot\cos\left(2tk\frac{\pi}{n} + \varepsilon_k\right)\left[\cos\left(2sj\frac{\pi}{n} + \varepsilon_j\right)\cdot\cos\left(2rk\frac{\pi}{n} + \varepsilon_k\right) + \cos\left(2rj\frac{\pi}{n} + \varepsilon_j\right)\cdot\cos\left(2sk\frac{\pi}{n} + \varepsilon_k\right)\right] \quad . \quad . \quad (16)$$

and there is another term from the same bonding cosine wave function orbital $[\psi_j(\cos)]$ and the antibonding sine wave function $[\psi_k(\sin)]$:

$$4\,\frac{\chi_j^2\cdot\chi_k^2}{(e_j - e_k)}\left[\cos\left(2tj\frac{\pi}{n} + \varepsilon_j\right)\cdot\sin\left(2tk\frac{\pi}{n} + \varepsilon_k\right)\left[\cos\left(2sj\frac{\pi}{n} + \varepsilon_j\right)\cdot\sin\left(2rk\frac{\pi}{n} + \varepsilon_k\right) + \cos\left(2rj\frac{\pi}{n} + \varepsilon_j\right)\cdot\sin\left(2sk\frac{\pi}{n} + \varepsilon_k\right)\right] \quad . \quad . \quad (17)$$

[9] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 275.

[10] Treibs, *Annalen*, 1952, **576**, 110; Treibs, Steinert, and Kirchhof, *ibid.*, 1953, **581**, 54; Anderson and Tazuma, *J. Amer. Chem. Soc.*, 1952, **74**, 3455; Nozoe, Mukai, and Murata, *ibid.*, 1954, **76**, 3352; Lloyd, *Chem. and Ind.*, 1953, 921; Hunter, Lloyd, Marshall, Price, and Rowe, *ibid.*, 1954, 1068.

Multiplying out (16) and (17), and summing, we have:

$$4\frac{\chi_j^2\cdot\chi_k^2}{(e_j-e_k)}\left[\cos\left(2tj\frac{\pi}{n}+\varepsilon_j\right)\cdot\cos\left(2sj\frac{\pi}{n}+\varepsilon_j\right)\cos 2(t-4)k\frac{\pi}{n}+\right.$$
$$\left.\cos\left(2tj\frac{\pi}{n}+\varepsilon_j\right)\cos\left(2rj\frac{\pi}{n}+\varepsilon_j\right)\cos 2(t-s)k\frac{\pi}{n}\right] \quad . \quad . \quad (18)$$

Another pair of terms arises from the bonding sine wave function orbital [$\psi_j$(sin)] and the antibonding cosine and sine wave function orbitals [$\psi_k$(cos) and $\psi_k$(sin)]. Summing as before, we have

$$4\frac{\chi_j^2\cdot\chi_k^2}{(e_j-e_k)}\left[\sin\left(2tj\frac{\pi}{n}+\varepsilon_j\right)\sin\left(2sj\frac{\pi}{n}+\varepsilon_j\right)\cdot\cos 2(t-r)k\frac{\pi}{n}+\right.$$
$$\left.\sin\left(2tj\frac{\pi}{n}+\varepsilon_j\right)\cdot\sin\left(2rj\frac{\pi}{n}+\varepsilon_j\right)\cos 2(t-s)k\frac{\pi}{n}\right] \quad . \quad . \quad (19)$$

Summing (18) and (19), we have

$$4\frac{\chi_j^2\cdot\chi_k^2}{(e_j-e_k)}\left[\cos 2(t-r)k\frac{\pi}{n}\cdot\cos 2(t-s)j\frac{\pi}{n}+\cos 2(t-s)k\frac{\pi}{n}\cdot\cos 2(t-r)j\frac{\pi}{n}\right] \quad (20)$$

Expressions such as (20) account for all terms except those involving the non-degenerate molecular orbitals[$j=0$, $k=(2\gamma+1)$]. The latter terms may also be written in this form, the contributions from the sine wave functions being zero. Since the sine factors themselves vanish, their $\chi$'s may be chosen arbitrarily and if we take them as equal to the $\chi$'s of the non-degenerate cosine wave functions, the above summation is still possible. Equation (4) is obtained from (20) by summation.

## Appendix 2

It is required to obtain equation (5) from equation (4). First consider the case when $j$ and $k$ are conjugate molecular orbitals; putting $k=[(2\gamma+1)-j]$ and $e_k=-e_j$ in (20) and expanding, we have

$$\frac{2\chi_j^2}{e_j}\left[\cos 2(t-s)j\frac{\pi}{n}\cdot\cos 2(t-r)j\frac{\pi}{n}\right]\left[\cos(t-r)\pi+\cos(t-s)\pi\right] \quad . \quad . \quad (21)$$

which, after the summation, is the first part of eqn. (5).

The remaining terms in $\pi_{t,rs}$ arise from the non-conjugate pairs of orbitals. Let the bonding pair conjugate with $k$ be $h(\neq j)$. Then $k=\{(2\gamma+1)-h\}$ and $e_k=-e_h$ and (20) becomes

$$4\frac{\chi_j^2\chi_h^2}{(e_j+e_h)}\left[\cos(t-r)\pi\cdot\cos 2(t-r)h\frac{\pi}{n}\cdot\cos 2(t-s)j\frac{\pi}{n}+\right.$$
$$\left.\cos(t-s)\pi\cdot\cos 2(t-s)h\frac{\pi}{n}\cdot\cos 2(t-r)j\frac{\pi}{n}\right] \quad . \quad . \quad (22)$$

and there is another term from the antibonding orbitals conjugate with $j$ and the bonding orbitals $h$. On replacement of $j$ by $h$ and $k$ by $\{(2\gamma+1)-j\}$ equation (20) becomes

$$4\frac{\chi_j^2\chi_h^2}{(e_j+e_h)}\left[\cos(t-r)\pi\cdot\cos 2(t-r)j\frac{\pi}{n}\cdot\cos 2(t-s)h\frac{\pi}{n}+\right.$$
$$\left.\cos(t-s)\pi\cdot\cos 2(t-s)j\frac{\pi}{n}\cdot\cos 2(t-r)h\frac{\pi}{n}\right] \quad . \quad . \quad (23)$$

Summing (22) and (23), we find

$$4\frac{\chi_j^2\chi_h^2}{(e_j+e_h)}\left[\cos(t-r)\pi+\cos(t-s)\pi\right]\left[\cos 2(t-r)h\frac{\pi}{n}\cos 2(t-s)j\frac{\pi}{n}+\cos 2(t-r)j\frac{\pi}{n}\cdot\cos 2(t-s)h\frac{\pi}{n}\right] \quad . \quad . \quad (24)$$

which, after the appropriate double summation, is the second part of eqn. (5).

## Appendix 3

It is required to obtain equation (14) from equation (13). Of the various terms arising in $\pi_{t,ss'}$, all except those involving the non-bonding molecular orbitals are analogous to those for the $(4\gamma+2)$ hydrocarbons and are easily shown to be

$$2\left[\left\{\cos(t-r)\pi+\cos(t-s)\pi\right\}\left\{\sum_{j=0}^{\gamma-1}\frac{\chi_j^4}{e_j}\cos 2(t-s)j\frac{\pi}{n}\cdot\cos 2(t-r)j\frac{\pi}{n}+\sum_{h=0}^{\gamma-2}\sum_{h=j+1}^{\gamma-1}2\frac{\chi_j^2\chi_h^2}{(e_j+e_h)}\cos 2(t-r)j\frac{\pi}{n}\cdot\cos 2(t-s)h\frac{\pi}{n}+\cos 2(t-s)j\frac{\pi}{n}\cdot\cos 2(t-r)h\frac{\pi}{n}\right\}\right] \quad . \quad . \quad (25)$$

To this must be added the terms involving the non-bonding molecular orbitals. Suppose the non-bonding molecular orbital having a cosine wave function to be doubly occupied in the perturbed sate. Then there will be one term from the $j$th bonding molecular orbital with a cosine wave function $[\psi_j(\cos)]$ and the sine wave function non-bonding molecular orbital $[\psi_\gamma(\sin)]$ which is

$$4\frac{\chi_j^2\chi_\gamma^2}{e_j}\left[\cos\left(2tj\frac{\pi}{n}+\varepsilon_j\right)\sin\left(t\frac{\pi}{2}+\varepsilon^\circ\right)\right]\left[\cos\left(2sj\frac{\pi}{n}+\varepsilon_j\right)\sin\left(r\frac{\pi}{2}+\varepsilon^\circ\right)+\cos\left(2rj\frac{\pi}{n}+\varepsilon_j\right)\sin\left(s\frac{\pi}{2}+\varepsilon^\circ\right)\right] \quad . \quad . \quad (26)$$

and there will be another term from the $j$th bonding molecular orbital with a sine wave function $[\psi_j(\sin)]$ and the sine wave function non-bonding molecular orbital $[\psi_\gamma(\sin)]$ of

$$4\frac{\chi_j^2\chi_\gamma^2}{e_j}\left[\sin\left(2tj\frac{\pi}{n}+\varepsilon_j\right)\sin\left(t\frac{\pi}{2}+\varepsilon^\circ\right)\right]\left[\sin\left(2sj\frac{\pi}{n}+\varepsilon_j\right)\sin\left(r\frac{\pi}{2}+\varepsilon^\circ\right)+\sin\left(2rj\frac{\pi}{n}+\varepsilon_j\right)\cdot\sin\left(s\frac{\pi}{2}+\varepsilon^\circ\right)\right] \quad . \quad . \quad (27)$$

Summing (26) and (27), we have

$$4\frac{\chi_j^2\chi_\gamma^2}{e_j}\sin\left(t\frac{\pi}{2}+\varepsilon^\circ\right)\left[\sin\left(r\frac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos 2(t-s)j\frac{\pi}{n}+\sin\left(s\frac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos 2(t-r)j\frac{\pi}{n}\right] \quad . \quad . \quad (28)$$

The other type of non-bonding molecular-orbital term in $\pi_{\cdot,rs'}$ is from the doubly occupied, cosine wave function non-bonding molecular orbital with the antibonding orbitals. Suppose the $k$th pair of antibonding orbitals to be conjugate with the $j$th bonding pair. Then on replacement $j$ by $\gamma$ and $k$ by $(2\gamma-j)$, the expression analogous to (28) is:

$$4\frac{\chi_j^2\chi_\gamma^2}{e_j}\cos\left(t\frac{\pi}{2}+\varepsilon^\circ\right)\left[\cos(t-r)\pi\cdot\cos\left(s\frac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos 2(t-r)j\frac{\pi}{n}+\cos(t-s)\pi\cdot\cos\left(r\frac{\pi}{2}+\varepsilon^\circ\right).\cos 2(t-s)j\frac{\pi}{n}\right] \quad . \quad . \quad (29)$$

XUM

Combining (28) and (29) and summing the result, we have

$$4\left[\sin\left(t\tfrac{\pi}{2}+\varepsilon^\circ\right)\cdot\sin\left(s\tfrac{\pi}{2}+\varepsilon^\circ\right)+\cos\left(t\tfrac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos\left(s\tfrac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos(t-r)\pi\right]\times\left[\sum_{j=0}^{\gamma-1}\left(\frac{\chi_j^2\cdot\chi_\gamma^2}{e_j}\right)\cos 2(t-r)j\frac{\pi}{n}\right]$$

$$+4\left[\sin\left(t\tfrac{\pi}{2}+\varepsilon^\circ\right)\cdot\sin\left(r\tfrac{\pi}{2}+\varepsilon^\circ\right)+\cos\left(t\tfrac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos\left(r\tfrac{\pi}{2}+\varepsilon^\circ\right)\cos(t-s)\pi\right]\times\left[\sum_{j=0}^{\gamma-1}\left(\frac{\chi_j^2\chi_\gamma^2}{e_j}\right)\cos 2(t-s)j\frac{\pi}{n}\right] \quad . \quad . \quad (30)$$

Combining (25) and (30) we have equation (14).

If the sine wave function non-bonding molecular-orbital is doubly occupied, the expression analogous to (30) is

$$4\left[\cos\left(t\tfrac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos\left(r\tfrac{\pi}{2}+\varepsilon^\circ\right)+\sin\left(t\tfrac{\pi}{2}+\varepsilon^\circ\right)\cdot\sin\left(r\tfrac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos(t-s)\pi\right]\times\left[\sum_{j=0}^{\gamma-1}\left(\frac{\chi_j^2\chi_\gamma^2}{e_j}\right)\cos 2(t-s)j\frac{\pi}{n}\right]$$

$$+4\left[\cos\left(t\tfrac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos\left(s\tfrac{\pi}{2}+\varepsilon^\circ\right)+\sin\left(t\tfrac{\pi}{2}+\varepsilon^\circ\right)\cdot\sin\left(s\tfrac{\pi}{2}+\varepsilon^\circ\right)\cdot\cos(t-r)\pi\right]\times\left[\sum_{j=0}^{\gamma-1}\left(\frac{\chi_j^2\chi_\gamma^2}{e_j}\right)\cos 2(t-r)j\frac{\pi}{n}\right] \quad . \quad . \quad (31)$$

The author is indebted to Professor M. J. S. Dewar for advice and encouragement.

ROYAL HOLLOWAY COLLEGE, ENGLEFIELD GREEN, SURREY. [*Received, September 27th,* 1957.]

---

## 208. $NH_2$-*Stretching Frequencies in Primary Amines.*

By W. J. ORVILLE-THOMAS, A. E. PARSONS, and C. P. OGDEN.

Precise frequency values have been obtained for the $NH_2$ stretching vibrations of a number of primary aliphatic and aromatic amines in solution and in the vapour state.

The greater intensity of the band due to the symmetric $NH_2$ vibration in aliphatic amines is explained in terms of hybridization changes at the nitrogen atom during vibration.

PRECISE values of N–H stretching frequencies are few since most of the published work has been carried out with the relatively low resolution afforded by a rock-salt prism.

Primary amines give rise to two infrared absorptions, associated respectively with the asymmetric and the symmetric vibration of the $NH_2$ group, $\nu_a(NH_2)$ and $\nu_s(NH_2)$.

The purpose of this study was to obtain precise values for these bands of monomeric primary amines in the vapour state and in carbon tetrachloride solution.

*Experimental.*—Amines (from British Drug Houses Ltd.) and "AnalaR" carbon tetrachloride used were dried and redistilled several times.

The measurements were made with a Grubb-Parsons G.S.2 double-beam grating spectrometer, the band centres being measured within $\pm 2$ cm.$^{-1}$.

The vapour studies were carried out in a multiple-reflection cell; [1] path lengths of 120, 240 cm., etc., were available and the cell could be heated to any desired temperature ±1°.

The experimental results are tabulated.

$NH_2$ *Bond-stretching frequencies* ($cm.^{-1}$) *in primary amines.*

| | Solution ($CCl_4$) | | Vapour (path length 120 cm.) | | |
|---|---|---|---|---|---|
| | $\nu_a(NH_2)$ | $\nu_s(NH_2)$ | $\nu_a(NH_2)$ | $\nu_s(NH_2)$ | Temp. |
| Methylamine | 3398 | 3344 | 3425 | 3360 | Room |
| *n*-Propylamine | 3390 | 3322 | 3410 | 3342 | Room |
| *iso*Propylamine | 3383 | 3319 | 3434 | 3332 | 32° |
| *n*-Butylamine | 3387 | 3324 | 3412 | 3348 | 75 |
| Aniline | 3481 | 3394 | 3497 | 3416 | 150 |
| α-Naphthylamine | 3472 | 3390 | 3478 | 3401 | 200 |
| β-Naphthylamine | 3475 | 3390 | 3484 | 3407 | 200 |

*Discussion.*—Except for methylamine, which as the first member of a homologous series is a special case, primary aliphatic amines give rise to two NH absorptions at 3387 ± 5 and 3322 ± 5 $cm.^{-1}$ in solution; the corresponding vapour values are 3425 ± 15 and 3340 ± 10 $cm.^{-1}$. For primary aromatic amines, however, they occur at higher frequencies, *viz.*, at 3476 ± 5 and 3391 ± 5 $cm.^{-1}$ in solution and at 3487 ± 10 and 3408 ± 10 $cm.^{-1}$ in the vapour state. The average frequency of $\nu_a(NH_2)$ and $\nu_s(NH_2)$ for aliphatic amines in the vapour state is 3382 $cm.^{-1}$ and for aromatic amines 3448 $cm.^{-1}$. This frequency difference can be explained in terms of the configuration of the nitrogen valency bonds.[2]

In methylamine, and it seems reasonable to suppose in other primary aliphatic amines also, the nitrogen valency bonds are pyramidal.[3] In aromatic amines the nitrogen σ-bonds are approximately planar in configuration.[4] The nitrogen atom is approximately $sp^3$-hybridized in aliphatic amines but is close to being $sp^2$-hydrized in aromatic amines. This increase in *s*-character of the nitrogen σ-bond-forming orbital in aromatic amines results in shorter and stronger NH bonds, which account for the higher values obtained for the $NH_2$ stretching frequencies.

Aniline appears to be the only primary aromatic amine previously studied in the vapour phase.[5,6] Williams, Hofstadter, and Herman,[6] using a cell of 22 cm. length at 150°, detected one weak absorption at 3573 $cm.^{-1}$ which they assigned to a NH vibration. In the present study, with a path length of 120 cm. and temperatures of 150—200°, both the $\nu_a(NH_2)$ and $\nu_s(NH_2)$ absorption bands were recorded for three aromatic amines (Table).

The $\nu_s(NH_2)$ band of aliphatic amines in the vapour state is much more intense than the $\nu_a(NH_2)$ band. To a good approximation the only nuclei taking part in the normal vibrations $\nu_a(NH)_2$) and $\nu_s(NH_2)$ are the nitrogen and the hydrogen atoms, and so the normal co-ordinates, $Q$, can be defined solely in terms of the changes in NH bond lengths during vibration.

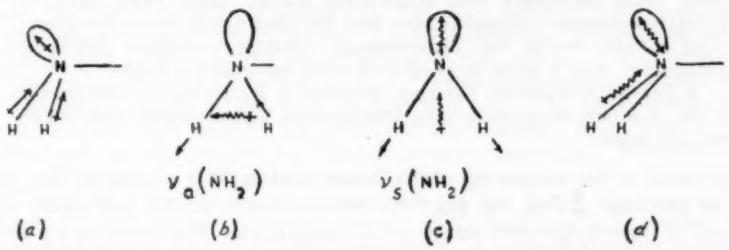
The intensity of an absorption band is proportional to the variation of molecular dipole moment, $\mu$, with the normal co-ordinate during vibration, *i.e.*, to $d\mu/dQ$. The electric moment of the $NH_2$ group can be divided into NH bond moments and the atomic dipole of the lone-pair electrons (Fig. *a*).

A consideration of the form of the $\nu_a(NH_2)$ vibration shows that the change in dipole moment (symbolized as +⟶) as the atoms oscillate is at right-angles to the symmetry axis of the $NH_2$ group (Fig. *b*); a change of equal magnitude, but along the symmetry axis, will occur for the $\nu_s(NH_2)$ vibration (Fig. *c*).

[1] White, *J. Opt. Soc. Amer.*, 1942, **32**, 285.
[2] Orville-Thomas and Parsons, Internat. Meeting European Mol. Spectroscopists, Freiburg i. Br., July, 1957.
[3] Nishikawa, Itoh, and Shimoda, *J. Chem. Phys.*, 1955, **23**, 1735.
[4] Coulson, "Valence," Oxford Univ. Press, 1952.
[5] Kettering and Sleator, *Physics*, 1933, **4**, 39.
[6] Williams, Hofstadter, and Herman, *J. Chem. Phys.*, 1939, **7**, 802.

It is now generally accepted that changes of hybridization occur at a central atom as the hybrid bonding orbitals tend to follow the vibrating outer atoms; [7] evidence has also been adduced for such changes during molecular rotations.[8] During the $\nu_a(NH_2)$ vibration the lengthening of one NH bond, which decreases its *s*-character, is exactly compensated by the gain in *s*-character of the other NH bond as it contracts. The percentage *s*-character of the lone-pair orbital remains unchanged and $d\mu/dQ$ depends almost entirely on the polar nature of the NH bond, which is small.[9] During the $\nu_s(NH_2)$ vibration there

*Variation of electric moment during* $NH_2$ *bond-stretching vibrations.*




will be a variation in the $s : p$ ratio of the nitrogen orbitals forming bonds to hydrogen. This will be off-set by a compensating change in the *s*-character of the lone-pair orbital; the atomic dipole will therefore vibrate in phase with the NH bonds. In this case, $d\mu/dQ$ has two components (Figs. *c* and *d*). One component is equal in magnitude to $d\mu/dQ$ for the $\nu_a(NH_2)$ vibration; the other, much larger contribution arises from the lone-pair electrons forming the atomic dipole: An estimate of the change in dipole moment during the $\nu_s(NH_2)$ vibration can be obtained by vector addition of the $NH_2$ bond moments and the atomic dipole when the NH bonds have their maximum and minimum lengths at the extremities of the vibration. This indicates that $d\mu/dQ$ will be greater for the $\nu_s(NH_2)$ than for the $\nu_a(NH_2)$ vibration and hence leads to a higher intensity for the $\nu_s(NH_2)$ band.

In accordance with expectations the same intensity anomaly is found for the vapour-state $NH_2$ stretching bands in hydroxylamine [10] and in *O*-methylhydroxylamine.[11]

In the vapour state formamide is planar,[12] the lone-pair electrons contributing to the delocalized $\pi$-bonding which embraces the OCN grouping. No atomic dipole is associated with the nitrogen atom and the $NH_2$ bands are of comparable intensity.[13] It is interesting to find a similar intensity ratio for the three aromatic amines studied. It seems then that evidence for the considerable $sp^2$-hybridized nature of the nitrogen atom in these compounds arises from intensity considerations as well as from the frequency values of the bands.

THE EDWARD DAVIES CHEMICAL LABORATORIES,
UNIVERSITY COLLEGE OF WALES, ABERYSTWYTH.
(C.P.O.) BASIC RESEARCH GROUP, THOMAS HEDLEY & CO., LTD.,
NEWCASTLE UPON TYNE, 1.
[*Received, October 17th*, 1957.]

[7] Linnett, *Ann. Reports*, 1953, **50**, 9.
[8] Orville-Thomas, Cox, and Gordy, *J. Chem. Phys.*, 1954, **22**, 1718; Cox, Gäumann, and Orville-Thomas, *Discuss. Faraday Soc.*, 1955, **19**, 52.
[9] Moffitt, *Proc. Roy. Soc.*, 1950, *A*, **202**, 548.
[10] Giguère and Liu, *Canad. J. Chem.*, 1952, **30**, 948.
[11] Spiers, personal communication.
[12] Kurland, *J. Chem. Phys.*, 1955, **23**, 2202.
[13] Evans, *ibid.*, 1954, **22**, 1228.

XUM

## 209. *Formation of Free Radicals during the Preparation of Organomagnesium Compounds in a Hydrocarbon Solvent.*

By D. Bryce-Smith and G. F. Cox.

Reactions of *n*-butyl chloride and *n*-butyl iodide (separately and mixed) with magnesium in *iso*propylbenzene have been examined. Evidence has been obtained for the intermediate production of free *n*-butyl radicals, mainly in reactions of the type $R_2Mg + 2RHal \longrightarrow 4R\cdot + MgHal_2$, analogous to those found previously with alkali-metal alkyls. High yields (85%) of *n*-butylmagnesium compounds have been obtained under certain conditions. With *n*-butyl iodide, the organometallic product is mainly di-*n*-butylmagnesium, with a small proportion of *n*-butylmagnesium iodide.

*n*-Butyltriphenylsilane has been prepared in high yield by the reaction of the di-*n*-butylmagnesium–*n*-butylmagnesium iodide reagent with chlorotriphenylsilane.

In previous work on the mechanism of the Wurtz reaction,[1,2] it was shown that free alkyl radicals are produced during the reactions between alkyl halides and alkali metals in benzene and in *iso*propylbenzene under certain conditions. The tendency for the metals to produce free *n*-butyl radicals from *n*-butyl iodide was found to increase in the order K < Na < Li. The present work concerns analogous experiments with magnesium.

### Experimental

*iso*Propylbenzene and alkyl halides were purified and dried by the methods previously described.[1] Reactions were carried out under oxygen-free nitrogen. Butane–butene mixtures were analysed by absorption of the butene in a saturated solution of nickel sulphate in concentrated sulphuric acid.

A typical experiment is described below. Other experiments given in Tables 1 and 2 were performed with the same weights of *iso*propylbenzene and *n*-butyl iodide (or the equivalent of *n*-butyl chloride), and the proportion of magnesium was varied.

Table 1. *Reactions between* n-*butyl iodide and magnesium in* iso*propylbenzene at* 130°.

| Expt. no. | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Equivs. of Mg [a] | 1·0 | 1·2 | 1·5 | 3·5 | 3·5 | 3·5 | 3·5 [b] |
| Heating period (hr.) | 20 [c] | 20 [c] | 2 | 2 | 2 | 2 | 12 |
| Yield (%) of *n*-$Bu_2Mg$ | 0 | 9·5 | 40·5 | 55·5 | *d* | *d* | 57·0 |
| ,, *n*-BuMgI | 0 | 2·5 | 4·5 | 17·5 | *d* | *d* | 13·5 |
| ,, total C–Mg material | 0 [c] | 12·0 | 45·0 | 73·0 | 72·5 | 85·5 | 70·5 |
| ,, *n*-$C_4H_{10}$ [f] | 47·5 | 34·5 | 18·0 | 8·5 | 4·5 | *d* | 6·5 |
| ,, *n*-$C_4H_8$ | 24·0 | 25·0 | 7·0 | 0·5 | 0·5 | *d* | 1·0 |
| ,, *n*-$C_8H_{18}$ | 29·0 | *d* | 15·0 | 16·0 | 13·5 | *d* | 21·0 |
| Yield $C_{12}H_{22}$ [g] | 18·5 | 11·0 | 7·5 | 3·0 | 3·6 | *d* | 3·5 |
| Titre *a* (ml.) | 0·1 | 2·2 | 7·2 | 11·8 | 11·7 | 13·8 | 11·4 |
| Titre *b* (ml.) [b] | 1·2 | 2·5 | 8·0 | 11·6 | 13·5 | *d* | 12·4 |
| Recovery (%) of $C_4$ material | 100·5 | *d* | 85·0 | 98·0 | 91·0 [f] | *d* | 99·0 |

[a]–[f] See text.

*Reaction between* n-*Butyl Iodide and Magnesium in* iso*Propylbenzene.*—*n*-Butyl iodide (13·00 g., 0·071 mole) was added during 30 min. with stirring to magnesium turnings (3·0 g., 0·123 g.-atom) in *iso*propylbenzene (36·5 g., 0·306 mole) at 130°. Reaction proceeded readily after a 10-min. induction period. Heating at 130° was continued for a further 1½ hr. Butane (8·5%) and butene (0·5%) were collected in a trap at −70°. After being kept for *ca.* 30 min., 1-ml. portions of the clear supernatant liquid and the stirred suspension were hydrolysed and titrated against 0·097N-hydrochloric acid: 11·8 and 11·6 ml. respectively were required, equivalent to a 73% yield of total organomagnesium compounds [titres (*a*) and (*b*) in the Tables]. Iodine

[1] Bryce-Smith, *J.*, 1956, 1603.
[2] *Idem*, *J.*, 1955, 1712.

in aliquot samples of the supernatant liquid was estimated as silver iodide in the usual way: 1 ml. gave 0·065 g. of silver iodide, equivalent to a yield of 17·5% of *n*-butylmagnesium iodide. By subtraction, the yield of di-*n*-butylmagnesium was 55·5%. The supernatant liquid gave a strong positive reaction in the test for organomagnesium compounds with Michler's ketone reagent.[3] After hydrolysis of the bulk of the product with dilute hydrochloric acid, the separated and dried organic material was fractionated, to give octane (0·63 g., 16%; estimated as previously described [1]) and 2 : 3-dimethyl-2 : 3-diphenylbutane (0·25 g., 3·0%), m. p. and mixed m. p. 118°. The total recovery of $C_4$ material was 98%.

*Notes to Table* 1: [a] One equivalent refers to the hypothetical reaction $2BuI + Mg \longrightarrow 2Bu^{\cdot} + MgI_2$. Two equivalents would theoretically be required to form butylmagnesium compounds. In expt. 6, magnesium powder (80—100 mesh) was used, and in the other experiments, magnesium turnings (<40 mesh). [b] This experiment demonstrates the effects attributable to any pyrolysis of the organomagnesium compounds. [c] These longer reaction periods were necessary to ensure complete reaction. The rather low recovery in expt. 3 suggests that this reaction may not have been quite complete after 2 hr. [d] No determination was made. [e] A negative reaction with Michler's ketone reagent was observed: in the other experiments, the reactions were strongly positive for organomagnesium compounds. The yields are based on titre *a*. [f] If allowance is made for butane produced by the reaction $Bu^n + C_6H_5{\cdot}CHMe_2 \longrightarrow n\text{-BuH} + C_6H_5{\cdot}CMe_2^{\cdot}$, the butane : butene ratios in expts. 1, 2, 3, and 5 approximate to unity. [g] 2 : 3-Dimethyl-2 : 3-diphenylbutane. The quoted yields refer to material of m. p. >114° and are based on *n*-butyl iodide. [h] These figures should be regarded as approximate owing to the experimental difficulty of obtaining satisfactory aliquot parts of the suspension. [i] Reaction with solid carbon dioxide gave *n*-valeric acid (29%), b. p. 180—185° (*p*-bromophenacyl ester m. p. and mixed m. p. 73°. Several sources quote m. p. 64° for this compound: others quote a m. p. close to 73°. On a previous occasion, we obtained crystals melting sharply at 63·5°: after 6 years, the sample was found to melt sharply at 73°. This seems to be a case of dimorphism. We have been unable to repeat the preparation of the lower-melting, and evidently less stable, form).

TABLE 2. *Reactions of* n-*butyl chloride and* n-*butyl iodide with magnesium* (3·5 *equiv.* : <40 *mesh*) *in* iso*propylbenzene.*

| | | | | | |
|---|---|---|---|---|---|
| Wt. % of $Bu^nCl$ | 100 | 100 | 100 | 85 |
| ,, $Bu^nI$ | 0 | 0 | 0 | 15 |
| Reaction temp. | 138—152° [a] | 132° | 110° [b] | 100° [c] |
| Heating period (min.) | 40 | 40 | 90 | 60 |
| Yield (%) of total C–Mg material | 25 | 35·5 | 0 | 61 |
| ,, $n\text{-}C_4H_{10}$ | 26 | *d* | 0 | 8·5 |
| ,, $n\text{-}C_4H_8$ | 3 | *d* | 0 | 1·5 |
| ,, $n\text{-}C_8H_{18}$ | 28 | 23 | 0 | 12 |
| ,, $C_{18}H_{22}$ [e] | 0·9 [f] | 0·65 | 0 | 0·9 |

[a–f] See text.

*Notes to Table* 2: [a] Reflux temperature. [b] Very little reaction occurred at this temperature. [c] Initiated at 135°. [d] Not determined. [e] 2 : 3-Dimethyl-2 : 3-diphenylbutane. [f] The high-boiling material which remained after removal of $C_{18}H_{22}$ by recrystallisation was oxidised by a slight excess of chromium trioxide in glacial acetic acid at 130° for 24 hr. Terephthalic acid (0·5%, based on $n\text{-}C_4H_9Cl$) was obtained, and estimation *via* the dithallous salt [4] showed that it contained not more than 1% of *iso*phthalic acid. This result is under further investigation.

*Preparation of* n-*Butyltriphenylsilane.*—The *n*-butylmagnesium reagent was prepared from *n*-butyl iodide (13·0 g., 0·071 mole) as in expt. 4, Table 1. Chlorotriphenylsilane (12·5 g., 0·043 mole) was added and the mixture was heated under reflux with stirring for 95 min. After cooling, excess of organomagnesium compounds was destroyed by the addition of dilute hydrochloric acid. The separated and dried organic layer was fractionated to remove *iso*propylbenzene. The addition of absolute ethanol to the residue gave colourless crystals of *n*-butyltriphenylsilane (11·5 g., 85·5%), m. p. 86°. Recrystallisation from absolute methanol raised the m. p. to 88° (Found: C, 83·5; H, 7·5. Calc. for $C_{22}H_{24}Si$: C, 83·45; H, 7·65%). Gilman,

[3] Gilman and Schulz, *J. Amer. Chem. Soc.*, 1925, **47**, 2002.
[4] Bryce-Smith, *Chem. and Ind.*, 1953, 244.

XUM

Benkeser, and Dunn [5] prepared this compound in 85% yield by the reaction of *n*-butyl-lithium with chlorotriphenylsilane, and reported m. p. 87·5—88°.

Several attempts were made to prepare tetra-*n*-butylsilane by a method analogous to the above, using silicon tetrachloride. Moderate yields of a product with b. p. close to the reported value were obtained; but analyses were always unsatisfactory (*e.g.*, Found: C, 77·75; H, 12·3. Calc. for $C_{16}H_{36}Si$: C, 74·9; H, 14·15%). Other material, presumably containing partially butylated compounds, was also obtained. After hydrolysis, this gave silicone-like oils.

## Discussion

Recently,[1] the production of 2 : 3-dimethyl-2 : 3-diphenylbutane was used to detect, and approximately to estimate, the free alkyl radicals which are formed during the reactions between alkyl halides and alkali metals in *iso*propylbenzene. It was shown in the case of lithium that the radicals arise from reactions of the type $RBr + RLi \longrightarrow 2R\cdot + LiBr$, and not from the initial reaction between the halide and the metal or from thermal decomposition of RLi. Kharasch and Urry [6] found that free radicals are formed during the reactions between certain alkyl halides and alkylmagnesium halides in the presence of catalytic quantities of cobalt halides. A chain mechanism was proposed, involving cobalt subhalides. A slower free-radical reaction which occurred in the absence of added catalyst was similarly suggested to involve magnesium subhalide produced by a reaction $RMgHal \longrightarrow R\cdot + MgHal$. More recently, Kharasch and Reinmuth [7] have made the alternative suggestion that a direct homolytic reaction can occur, *viz.*, $RMgHal + RHal \longrightarrow 2R\cdot + MgHal_2$.* This reaction is analogous to that found [1] to occur with alkyllithium compounds. The present work has shown that *n*-butyl iodide produces free *n*-butyl radicals to approximately the same extent with magnesium as with lithium: the yields of 2 : 3-dimethyl-2 : 3-diphenylbutane under comparable conditions were 18·5 and 17% respectively.

The free-radical reactions which could be involved when *n*-butyl iodide reacts with magnesium are indicated in the following scheme:




The possibility that reaction (5) occurs under the present conditions is excluded by the result of expt. 7, Table 1. The yields of *n*-butylmagnesium compounds and of 2 : 3-dimethyl-2 : 3-diphenylbutane were almost unchanged by increasing the period of heating at 130° from 2 to 12 hours.

In considering reactions (1), (2), (3), and (4) as possible competing fates for *n*-butyl iodide, one is dealing with a competition between heterogeneous and homogeneous reactions, the rate of (4) depending also on the heterogeneous reaction (3). It seems a valid assumption that the relative rates of (1) and (3) should be independent of the surface area of the magnesium and the weight ratio of *n*-butyl iodide and magnesium. The 85·5% yield of *n*-butylmagnesium compounds obtained in expt. 6, Table 1, indicates that (3) must be much faster than (1): and some of the 14·5% deficiency of *n*-butylmagnesium compounds can certainly be attributed to the occurrence of reaction (4). Further, increasing the

* But contrast ref. 7, p. 1059.

[5] Gilman, Benkeser, and Dunn, *J. Amer. Chem. Soc.*, 1950, **72**, 1689.
[6] Kharasch and Urry, *J. Org. Chem.*, 1948, **13**, 101.
[7] Kharasch and Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, New York, 1954; Constable, London, p. 131.

proportion of magnesium (*i.e.*, increasing the available surface area) from 1 to 3·5 equivalents increased the yield of *n*-butylmagnesium compounds from 0 to 73%, or, when magnesium powder was used, to 85·5%; reactions (1), (2), and (3) thereby become more important than reaction (4). At the same time, the yield of 2 : 3-dimethyl-2 : 3-diphenylbutane fell from 18·5 to *ca.* 3%. The radical yield * must therefore be mainly determined by the extent of reaction (4), rather than reactions (1) and (2). The deficiency from quantitative in the yields of *n*-butylmagnesium compounds may be attributed mainly to the homolytic reaction (4) (and related heterolytic coupling and elimination reactions [1]) rather than to reactions (1) and (2), and the yields of 2 : 3-dimethyl-2 : 3-diphenylbutane are approximately proportional to this deficiency. The precision of the results does not, however, justify the complete exclusion of reactions (1) and (2) as minor radical contributors. It seems probable that di-*n*-butylmagnesium and *n*-butylmagnesium iodide are both involved in reaction (4), but the question whether they are equally involved must remain open.

*Preparation of Organomagnesium Compounds in* iso*Propylbenzene.*—*iso*Propylbenzene was used as a solvent in this work because of its ability to function as a radical detector; but it has also been found to be an unexpectedly good solvent for the preparation of *n*-butylmagnesium compounds under certain conditions. The numerous attempts to prepare Grignard reagents in non-donor media have been summarised by Kharasch and Reinmuth.[8] Usually, the addition of small quantities of an ether or tertiary amine has been found necessary in order to obtain acceptable yields in conveniently short reaction periods. Tschelinzeff [9] reported the preparation of several Grignard reagents at approximately 140° in the absence of added solvent and catalyst: Schlenk [10] also obtained these in benzene, the reactions requiring two months for completion. In *iso*propylbenzene, we find that the main product with *n*-butyl iodide is di-*n*-butylmagnesium, with a much smaller proportion of *n*-butylmagnesium iodide. By use of a 75% excess of magnesium powder (rather than turnings), a combined yield of 85·5% was obtained (Table 1, expt. 6) identical with that reported by Gilman *et al.*[11] for a conventional preparation of *n*-butylmagnesium iodide in ether. Use of a more finely divided magnesium powder would probably give an even higher yield.

The use of *n*-butyl chloride was also investigated, and the results are summarised in Table 2. The radical yields were much lower than from the iodide. Yields of organomagnesium compounds were also lower, although a 61% yield was obtained from a mixture of *n*-butyl chloride and a little *n*-butyl iodide. This yield also could almost certainly be improved upon by the use of a more finely divided magnesium.

The possible synthetic usefulness of these new reagents has been suggested by the preparation of *n*-valeric acid (29% yield) from carbon dioxide, and of *n*-butyltriphenylsilane (85·5% yield) from chlorotriphenylsilane. A reaction with silicon tetrachloride, expected to give tetra-*n*-butylsilane, gave a product which we were unable to obtain pure.

One of us (G. F. C.) thanks Messrs. Albright and Wilson Limited for a maintenance grant.

Department of Chemistry,
The University, Reading, Berks. [*Received, August 20th*, 1957.]

* This does not include any radicals which might be captured by the magnesium, but refers to radicals which are sufficiently "free" to react with the solvent.

[8] *Op. cit.*, pp. 50 *et seq.*
[9] Tschelinzeff, *Ber.*, 1904, **37**, 4534.
[10] Schlenk, *Ber.*, 1931, **64**, 739.
[11] Gilman, Zoellner, and Dickey, *J. Amer. Chem. Soc.*, 1929, **51**, 1576, 1583.

XUM

## 210. *Researches on Acetylenic Compounds. Part LX.* The Synthesis of Three Natural Polyacetylenic Hydrocarbons.*

By E. R. H. Jones, L. Skattebøl, and M. C. Whiting.

The hydrocarbons (III), where R = *trans*-Me·CH=CH, *cis*-Me·CH=CH, and Me·C≡C–, have been synthesised and shown to be identical with compounds isolated from *Correopsis* species.

From plants of the Compositae family a large number of polyacetylenic compounds has been isolated by N. A. and J. S. Sørensen and their co-workers. These include [1] a group of $C_{13}$ compounds characterised by the presence of a methyl or acetoxymethyl group at one end of the molecule, and at the other either a vinyl group or an unsubstituted benzene ring. The conclusion is almost inescapable that the benzene ring is formed *in vivo* either by a novel cyclisation of a polyenyne system or from a common intermediate. The acyclic members of this group are easily the most unsaturated compounds yet encountered in Nature (*e.g.*, $C_{13}H_6$), and are among the most unstable substances ever isolated. Since they are present in extremely minute quantities, their necessarily tentative identification represents a technical *tour de force*, and requires confirmation by synthesis, for which problems of scale do not arise. Indeed, one of these hydrocarbons, originally formulated [1] as divinyltetra-acetylene (dodeca-1 : 11-dienetetrayne), has been shown by the synthesis of the latter [2] and a consideration of the spectroscopic evidence to be, in all probability, *trans*-trideca-1 : 11-diene-3 : 5 : 7 : 9-tetrayne (III; R = *trans*-Me·CH=CH). We now describe synthetical confirmation of this structure, the synthesis of the corresponding *cis*-isomer which has permitted recognition of this compound as being present, together with the *trans*-form, in a garden species of *Correopsis*, and the synthesis of tridec-1-ene-3 : 5 : 7 : 9 : 11-pentayne (III; R = Me·C≡C), isolated from *Helipterum* species.

For the synthesis of unsymmetrical acetylenic hydrocarbons the oxidative cross-coupling reaction is inherently unsuitable because of the similarity of physical properties between the desired product and its symmetrical analogues, while the approach of Cook, Jones, and Whiting,[3] requiring the removal of hydrogen chloride from terminal groupings in a polyacetylenic dichloride R·CHCl·[C≡C]$_n$·CHClR′, was known to proceed in very low yield for large values of $n$. We therefore decided to use the modification employed by Bohlmann [4] for the preparation of the hydrocarbons $Me_3C·[C{\equiv}C]_n·CMe_3$ ($n$ = 5, 6, and 7), in which the two –CHCl– groups are located in non-terminal positions. This requires the preparation of an unsymmetrical glycol, *e.g.*, R·C≡C·CH(OH)·C≡C·CH(OH)·C≡C·R′, which can be prepared efficiently only by a two-stage route from the two appropriate αβ-acetylenic aldehydes and acetylene. Since the alkali-metal acetylides (at least, under normal conditions) merely polymerise αβ-acetylenic aldehydes, and the latter are likely to interact with the solvent in liquid ammonia experiments, it was first necessary to develop the method recently described for preparing and using ethynylmagnesium bromide.[5]

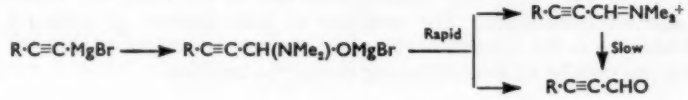
αβ-Acetylenic aldehydes have usually been prepared *via* the acetals by Grignard condensations with ethyl orthoformate,[6] but as overall yields are low the use of dimethylformamide [7] was investigated. The aldehydes were obtained directly, without any secondary alcohol being formed; this contrasts with the analogous reaction with ethyl formate, where the initial complex, R·C≡C·CH(OEt)·O·MgBr, can lose an ethoxide ion and

* Part LIX, preceding paper.

[1] J. S. Sørensen and N. A. Sørensen, *Acta Chem. Scand.*, 1954, **8**, 1741; J. S. Sørensen, Holme, Borlaug, and N. A. Sørensen, *ibid.*, p. 1769; J. S. Sørensen and N. A. Sørensen, *ibid.*, p. 1763.
[2] Jones, Thompson, and Whiting, *ibid.*, p. 1944.
[3] Cook, Jones, and Whiting, *J.*, 1952, 2883.
[4] Bohlmann, *Chem. Ber.*, 1953, **86**, 63, 657.
[5] Jones, Skattebøl, and Whiting, *J.*, 1956, 4765.
[6] Viguier, *Ann. Chim.* (*France*), 1913, **28**, 447; Lunt and Sondheimer, *J.*, 1950, 3364.
[7] Bouveault, *Bull. Soc. chim. France*, 1904, **31**, 1322; Sicé, *J. Amer. Chem. Soc.*, 1953, **75**, 3697.

XUM

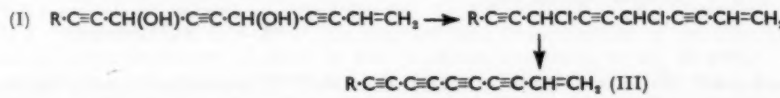
react further. Decomposition of the Grignard complex, however, required an inverse-addition technique, as otherwise dimethylamine, formed locally where basic conditions prevailed, at once added to the acetylenic aldehyde. It was noticed that some of the aldehyde was formed immediately on decomposition of the complex, while the rest became extractible by ether only after the clear acid solution had been kept for some time. Presumably the aldehyde and the dimethylimonium cation were produced simultaneously,




and the latter was only slowly hydrolysed to the former. Similar considerations may well apply in other cases of the Bouveault aldehyde synthesis.[7]

Aldehydes, R·C≡C·CHO, were readily obtained from hex-1-yne and *cis*- and *trans*-pent-2-en-4-yne [8] by this method in *ca.* 50% yields. From penta-1 : 3-diyne,[9] however, the aldehyde, though obtained in a crude state in fair yield, decomposed explosively on distillation at 70°/15 mm.; only a small amount of (crystalline) product was isolated. Vinylacetylene gave low and very variable yields, apparently because the coarsely divided state of the Grignard complex in this case rendered the reverse-addition technique for decomposition less effective. The corresponding alcohol was conveniently obtained from sodiovinylacetylene, prepared *in situ*,[10] and formaldehyde; it underwent oxidation to the required aldehyde with manganese dioxide in methylene dichloride [11] in fair yield; this procedure is much more satisfactory than the Grignard reaction in this case.

Like hept-2-ynal,[5] pent-4-en-2-ynal and the two stereoisomers of hex-4-en-2-ynal readily gave ethynylcarbinols on treatment with ethynylmagnesium bromide in tetrahydrofuran. Condensation of the alcohols with the appropriate aldehydes gave the three $C_{13}$ glycols (I; R = *cis*- and *trans*-Me·CH=CH and Me·C≡C); the difficulty of handling hexa-2 : 4-diynal made it preferable to use this in the second stage of the condensation, whereas the hexenynals were employed in the first. Although the glycols (I), after




chromatographic purification, were apparently mixtures of stereoisomers, we preferred to accept loss by crystallising them in order to ensure the maximum purity of the later products, which were bound to be intractable. Treatment with thionyl chloride in ether at 5° gave, in each case, a dichloride (II) which was dehydrochlorinated with potassium ethoxide in ethanol [4] at about −30°, the polyacetylenic hydrocarbons then being isolated chromatographically.

*trans*-Trideca-1 : 11-diene-3 : 5 : 7 : 9-tetrayne (III; R = Me·CH=CH) crystallised readily, and was compared directly with a sample of the hydrocarbon from *Correopsis* roots [1] sent as a solution in hexane from Trondheim. Except that it had proved possible to obtain a slightly purer sample of the latter, the two were readily shown to be identical by comparison of ultraviolet and infrared spectra (cf. Fig. 1).

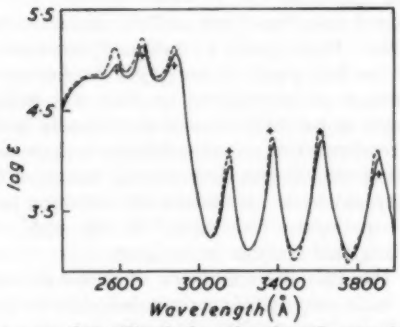
*cis*-Trideca-1 : 11-diene-3 : 5 : 7 : 9-tetrayne could not be induced to crystallise, but by chromatography it was brought to a state of approximate purity (as analytical data could not be obtained, and even direct weighing of samples for spectroscopic determination was impossible, one cannot be more precise). Its ultraviolet spectrum was almost identical

[8] Allan and Whiting, *J.*, 1953, 3314.
[9] Cook, Jones, and Whiting, *J.*, 1952, 2883.
[10] Croxall and Van Hook, *J. Amer. Chem. Soc.*, 1954, **76**, 1700.
[11] Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094.

XUM

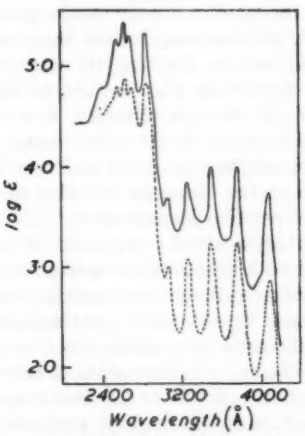
with that of the *trans*-isomer, but its infrared spectrum differed, as expected, especially in the substitution of an intense band at 713 cm.$^{-1}$ (*cis*) for one at 945 cm.$^{-1}$ (*trans*). This spectrum agreed exactly—in several minor as well as in the main bands—with that of a non-crystalline fraction separated chromatographically from the *trans*-isomer in the extracts of *Correopsis* roots [12] (this is the spectrum published by Sørensen and Sørensen [1]). Owing to the use of carbon tetrachloride as solvent, the bands most characteristic stereochemically, in the 670—1000 cm.$^{-1}$ region, were not, at the time, well observed for the naturally derived compounds. The presence of both isomers of trideca-1 : 11-diene-3 : 5 : 7 : 9-tetrayne in the extracts of this plant can now be recognised, but the possibility remains that one may be an artefact arising during the isolation.

FIG 1




– – – – *Crystalline hydrocarbon from* Correopsis *species.*
——— *Synthetic* trans-*trideca*-1 : 11-*diene*-3 : 5 : 7 : 9-*tetrayne.*
+ + + *Synthetic* cis-*trideca*-1 : 11-*diene*-3 : 5 : 7 : 9-*tetrayne* (*maxima only*).

FIG. 2.




– – – – *Crystalline hydrocarbon from* Helipterum *species.*
——— *Synthetic tridec*-1-*ene*-3 : 5 : 7 : 9 : 11-*pentayne.*

Tridec-1-ene-3 : 5 : 7 : 9 : 11-pentayne (III; R = Me·C≡C) crystallised readily but was extraordinarily unstable to light. The ultraviolet absorption spectrum (Fig. 2) is considerably more intense than that recorded for the natural hydrocarbon by Sørensen, Holme, Borlaug, and Sørensen.[1] It is also more intense than that of a specimen isolated in Oxford from a hexane solution of a concentrate supplied by Professor Sørensen. Despite the discrepancies in intensity, the very characteristic fine structure (especially the triple peak at 2400—2500 Å, an exceptional feature) leaves no doubt that the two substances responsible for this spectrum were identical. Similarly, the infrared spectrum of the best specimen of the natural hydrocarbon showed strong bands in the aliphatic C–H and the carbonyl stretching regions; but the characteristic and unusual triple C≡C stretching frequency at 2105, 2180, and 2215 cm.$^{-1}$, and the C–H out-of-plane deformation modes of the vinyl group were common to the two spectra, and also to that already published.[1]

Ultraviolet absorption spectra for the intermediates employed are in the annexed Table. Infrared spectra were as expected. To the generalisations of Allan, Meakins, and Whiting [13] on compounds of these types we would add that conjugation with an acetylenic linkage moves the C=O stretching band in aldehydes to about 1660—1665 cm.$^{-1}$, and that in the C–H out-of-plane deformation, the usual bands at 910 and 990 cm.$^{-1}$ for vinyl groups are displaced to about 920 cm.$^{-1}$ (rather variable) and 970 cm.$^{-1}$.

[12] J. S. Sørensen and N. A. Sørensen, personal communications.
[13] Allan, Meakins, and Whiting, *J.*, 1955, 1874.

*Ultraviolet absorption maxima of intermediates.*

*Vinylacetylenic aldehydes,* R·C≡C·CHO, *and their derivatives.*

| R = | $CH=CH_2$ | | Me·CH=CH (*t*) | | Me·CH=CH·(*c*) | | Me·C≡C | |
|---|---|---|---|---|---|---|---|---|
| | λ (Å) | $10^{-3}\varepsilon$ | λ (Å) | $10^{-3}\varepsilon$ | λ (Å) | $10^{-3}\varepsilon$ | λ (Å) | $10^{-3}\varepsilon$ |
| Aldehyde (hexane) ..... | 2520 | 10·9 | 2540 | 10·5 | 2560 | 8·3 | | |
| | 2640 | 10·4 | 2620 | 13·6 | 2640 | 10·7 | | |
| | | | 2740 | 11·9 | 2765 | 9·7 | | |
| Semicarbazone (alcohol) ... | 2830 | 23 | 2900 | 22·6 | 2905 | 26·2 | 2890 | 21·9 |
| | | | | | | | 3045 | 22·8 |
| Ethynylcarbinol (alcohol)... | 2235 | 9·5 | 2285 | 14·2 | 2270 | 12·6 | | |
| | 2330 | 7·5 | | | | | | |
| *Glycols* (I) *in alcohol.* | | | | | | | | |
| | | | 2250 | 27·0 | 2245 | 23·5 | 2240 | 12·7 |
| | | | 2310 * | 25·0 | 2325 * | 20·8 | 2340 | 10·5 |

* Inflexion.

## Experimental

General precautions necessary for dealing with polyacetylenic compounds were described in Part XXXIX.[9] The highly unsaturated hydrocarbons (III) were far too unstable for carbon and hydrogen determinations, and were therefore characterised by ultraviolet and infrared absorption spectra.

*Hept-2-ynal.*—A solution of hex-1-yne (20·5 g.) in dry ether (50 c.c.) was added dropwise to one of ethylmagnesium bromide in ether (150 c.c.), prepared from magnesium (6 g.) and an excess of ethyl bromide. The mixture was heated under reflux for 1 hr., transferred to a dropping-funnel, and added, during 1 hr., to a stirred solution of dimethylformamide (55 g.) in dry ether (100 c.c.) with external cooling (ice–salt). After being stirred for a further hour at 20° the resultant fine suspension was poured gradually into vigorously stirred 5% sulphuric acid (1 l.). After 18 hr., extraction with ether, evaporation of the solvent through a short Fenske column, and distillation gave the aldehyde (14·1 g., 51%), b. p. 54—55°/16 mm., $n_D^{20}$ 1·4516 (Goebel and Wenzke [14] give b. p. 61·8—62·5°/18 mm., $n_D^{25}$ 1·4499).

trans-*Hex-4-en-2-ynal.*—*trans*-Pent-2-en-4-yne (15 g.) similarly gave this *aldehyde* (10·8 g., 50%), b. p. 50—51°/14 mm., $n_D^{17}$ 1·5246 (Found: C, 76·6; H, 6·55. $C_6H_6O$ requires C, 76·6; H, 6·4%), which solidified at −25°. The *semicarbazone* formed plates, m. p. 150—156°, from aqueous methanol (Found: C, 55·4; H, 6·2. $C_7H_9ON_3$ requires C, 55·65; H, 6·2%).

cis-*Hex-4-en-2-ynal.*—*cis*-Pent-2-en-4-yne (15 g.) similarly gave this *aldehyde* (11·0 g., 51%), b. p. 40—41°/14 mm., $n_D^{20}$ 1·5133 (Found: C, 76·55; H, 6·55%). Its *semicarbazone* formed plates, m. p. 173—175°, from aqueous methanol (Found: C, 55·35; H, 6·1%).

*Pent-4-en-2-yn-1-ol.*—1 : 4-Dichlorobut-2-ene (125 g.) was added slowly to a stirred suspension of sodamide, prepared from sodium (64 g.) in liquid ammonia (1·5 l.) in a vacuum-flask. Dry paraformaldehyde (30 g.) was added, and the mixture was stirred for 40 hr., then transferred to a stainless-steel bucket, where most of the ammonia was allowed to evaporate. Extraction with ether, evaporation of the latter through a 10 cm. Fenske column, and distillation gave pent-4-en-2-yn-1-ol (23 g., 28%), b. p. 55—58°/17 mm., $n_D^{22}$ 1·4961 (Gverdtsiteli [15] gives b. p. 55—58°/10 mm., $n_D^{20}$ 1·4988).

*Pent-4-en-2-ynal.*—(*a*) An excess of vinylacetylene [16] was passed in a stream of nitrogen into a solution of ethylmagnesium bromide, prepared in ether (350 c.c.) from magnesium (12 g.) with ice-cooling. After being heated under reflux the solution was added with stirring to a solution of dimethylformamide (95 g.) in ether (150 c.c.) during 2 hr.; the complex separated in a coarsely aggregated, rather variable form. Decomposition with 5% sulphuric acid, as above, and isolation of the product gave the crude aldehyde (7·6 g., 19%, or less), b. p. 65—66°/100 mm., $n_D^{17}$ 1·4962.

(*b*) Pent-4-en-2-yn-1-ol (20 g.) in methylene dichloride (750 c.c.) was shaken with active manganese dioxide (200 g.). Filtration, evaporation of the solvent through a 10 cm. Fenske column, and distillation of the residue gave the aldehyde (5·9 g., 30%), b. p. 65°/100 mm., $n_D^{19}$

[14] Goebel and Wenzke, *J. Amer. Chem. Soc.*, 1937, **59**, 2301.
[15] Gverdtsiteli, *Doklady Akad. Nauk S.S.S.R.*, 1948, **60**, 57.
[16] Eglinton and Whiting, *J.*, 1950, 3650.

1·5015, probably purer than the specimen described above. Prepared by either route this compound formed a *semicarbazone*, m. p. 135—151° (decomp.) (Found: C, 52·25; H, 5·15. $C_8H_7ON_3$ requires C, 52·5; H, 5·1%). The aldehyde itself showed the expected ultraviolet and infrared absorption spectra (see above), but proved very unstable.

*Hexa-2 : 4-diynal.*—A solution of ethylmagnesium bromide, prepared in ether from magnesium (4·8 g.), was treated with penta-1 : 3-diyne (12 g.) and added to dimethylformamide (40 g.), and the product was isolated as described above. On distillation 2·6 g. of a liquid, b. p. 67—70°, were obtained; then, with the bath-temperature at about 80°, the remainder of the product exploded violently. No attempt was made to analyse the aldehyde, which crystallised at −15°, but a *semicarbazone* (decomp. at 173°) was obtained (Found: C, 56·4; H, 4·85. $C_7H_7ON_3$ requires C, 56·35; H, 4·75%).

*Nona-1 : 4-diyn-3-ol.*—A suspension of ethynylmagnesium bromide [5] was prepared from magnesium (4·8 g.) in tetrahydrofuran (200 c.c.) and cooled to 0°. A solution of hept-2-ynal (15 g.) in tetrahydrofuran (20 c.c.) was added with stirring during 1 hr., with ice-cooling, and the mixture was then stirred for 18 hr. at 20°. Decomposition with saturated ammonium chloride solution and isolation with ether gave the *alcohol* (15·8 g., 85%), b. p. 69°/0·5 mm., $n_D^{19}$ 1·4730 (Found: C, 79·6; H, 8·95. $C_9H_{12}O$ requires C, 79·4; H, 8·9%).

trans-*Oct-6-ene-1 : 4-diyn-3-ol.*—*trans*-Hex-4-en-2-ynal (16·2 g.) and ethynylmagnesium bromide, prepared from magnesium (6 g.), similarly gave this *alcohol* (17·7 g., 86%), b. p. 53—54°/0·05 mm., $n_D^{21}$ 1·5188 (Found: C, 79·5; H, 6·65. $C_8H_8O$ requires C, 80·0; H, 6·65%).

cis-*Oct-6-ene-1 : 4-diyn-3-ol.*—Similarly prepared from *cis*-hex-4-en-2-ynal (9·9 g.) and magnesium (3·6 g.), this *alcohol* (10·7 g., 85%) had b. p. 44—45°/0·05 mm., $n_D^{18}$ 1·5162 (Found: C, 80·2; H, 6·85%).

*Hept-6-ene-1 : 4-diyn-3-ol.*—Pent-4-en-2-ynal (5·8 g.) was condensed with ethynylmagnesium bromide, prepared from magnesium (3·0 g.) as above. The *alcohol* (5·4 g., 70%) had b. p. 41—42°/1 mm., $n_D^{15}$ 1·5138 (Found: C, 79·45; H, 5·7. $C_7H_6O$ requires C, 79·25; H, 5·7%). The lower yield obtained in this case may reflect lower purity of the starting material; on the other hand, this alcohol, unlike its analogues, polymerised extensively when stored at −15° for a few weeks.

trans-*Trideca-1 : 11-diene-3 : 6 : 9-triyne-5 : 8-diol* (I; R = Me·CH=CH).—A solution of *trans*-octa-1 : 4-diyn-3-ol (6 g.) in tetrahydrofuran (25 c.c.) was added during 1 hr. to an ice-cooled solution of ethylmagnesium bromide, prepared from magnesium (2·7 g.) in tetrahydrofuran (50 c.c.). After an additional hour, the temperature was lowered to *ca.* −15° while a solution of pent-4-en-2-ynal (3·3 g.) in tetrahydrofuran (5 c.c.) was added during 30 min. The mixture was stirred at 0° for 7 hr. Decomposition with ammonium chloride solution and isolation with ether gave a partly crystalline product which was chromatographed on deactivated alumina. The ether eluate was crystallised from benzene, giving the *glycol* (3·1 g., 38%) as needles, m. p. 123—124° (Found: C, 77·7; H, 6·1. $C_{13}H_{12}O_2$ requires C, 78·0; H, 6·05%). A polymorphic form, m. p. 76—78°, was obtained from light petroleum.

cis-*Trideca-1 : 11-diene-3 : 6 : 9-triyne-5 : 8-diol* (I; R = Me·CH=CH) was similarly prepared by condensing *cis*-octa-1 : 4-diyn-3-ol (3·0 g.) with pent-4-en-2-ynal (1·8 g.). Chromatography on deactivated alumina gave an ether eluate which was, with considerable difficulty, induced to crystallise under benzene–light petroleum (1·2 g., 27%, m. p. 80—85°). After recrystallisation the *diol* formed needles, m. p. 88° (Found: C, 78·0; H, 6·05%).

*Tridec-1-ene-3 : 6 : 9 : 11-tetrayne-5 : 8-diol* (I; R = Me·C≡C) was similarly prepared by condensing hept-6-ene-1 : 4-diyn-3-ol (2·7 g.) with crude hexa-2 : 4-diynal (2·3 g., as above). After chromatography, trituration with benzene gave a solid (850 mg.), which on crystallisation from benzene–light petroleum yielded the *glycol*, m. p. 111—114° (slight decomp.) (Found: C, 77·5; H, 5·25. $C_{13}H_{10}O_2$ requires C, 78·8; H, 5·25%).

trans-*Trideca-1 : 11-diene-3 : 5 : 7 : 9-tetrayne* (III; R = Me·CH=CH).—A solution of *trans*-trideca-1 : 11-diene-3 : 6 : 9-triyne-5 : 8-diol (1·2 g.) in dry ether (3 c.c.) was treated with thionyl chloride (1·5 c.c.) at 5° for 2 hr. Addition of water and more ether gave an upper phase which was dried and evaporated at room temperature, leaving a dark liquid which, without purification, was dissolved in dry ether (10 c.c.). This solution was added dropwise to a stirred solution of potassium ethoxide, prepared from potassium (1·5 g.) in ethanol (25 c.c.) and cooled to −30°. The mixture was stirred for 30 min., the bath-temperature being allowed to rise to 0°. Addition of water and isolation with ether gave a semi-solid product which was chromatographed on activated alumina; the light petroleum eluates were evaporated to *ca.* 5 c.c. and set aside

at −30°, a solid separating which, crystallised several times from pentane, gave the hydrocarbon (*ca.* 25 mg.) as pale yellow needles, which decomposed (without melting) above 40° and rapidly became brown in diffused daylight, even at −5°. Catalytic hydrogenation resulted in an uptake of 10·1 mols.

cis-*Trideca*-1 : 11-*diene*-3 : 5 : 7 : 9-*tetrayne* (III; R = Me·CH=CH).—The corresponding *cis*-glycol (880 mg.) and thionyl chloride (1 c.c.) gave a crude dichloro-compound, which was treated with potassium ethoxide (from 1·5 g. of potassium) as described above. The hydrocarbon (*ca.* 20 mg.) was a liquid, even after repeated chromatography, but its ultraviolet and infrared spectra agreed with the postulated structure.

*Tridec*-1-*ene*-3 : 5 : 7 : 9 : 11-*pentayne* (III; R = Me·C≡C).—The tetra-acetylenic glycol (800 mg.) and thionyl chloride (1 c.c.) in ether (2 c.c.) gave a crude dichloride, which was added to a solution of potassium ethoxide, prepared from potassium (1 g.) in ethanol (15 c.c.), at −40° for 15 min. Isolation and then chromatography gave a yellow zone, and when this was eluted with light petroleum a solid was readily obtained. Several recrystallisations from pentane gave the hydrocarbon (*ca.* 100 mg.) as yellow needles, extraordinarily sensitive to light; the ultraviolet absorption spectrum illustrated characterises this substance and proves its identity with the natural product.

THE DYSON PERRINS LABORATORY,
OXFORD UNIVERSITY,

[*Received, October 8th,* 1957.]

---

## 211. *The Hemicelluloses of European Larch* (Larix decidua). *Part I. The Constitution of a Xylan.*

By G. O. ASPINALL and J. E. MCKAY.

Larch hemicellulose fractions are composed of residues of D-xylose, L-arabinose, D-mannose, D-glucose, D-galactose, and 4-*O*-methyl-D-glucuronic acid. From methylation and other experiments it is concluded that there is present a xylan containing unbranched chains of *ca.* 100 1 : 4-linked β-D-xylopyranose residues with every fifth or sixth residue carrying a terminal 4-*O*-methyl-D-glucuronic acid residue linked through position 2, and a smaller proportion of xylose residues carrying, on position 3, side-chains terminated by L-arabofuranose residues.

LARCHES are the only common deciduous conifers. They differ chemically from other coniferous woods in containing a much higher proportion of galactose-containing polysaccharides. The galactans are easily extracted with water and those from European [1] and Western [2] larches have been extensively studied. It was of interest to extend the investigations to the alkali-soluble hemicelluloses and this paper describes the structure of a xylan from European larch wood (*Larix decidua*).

Larch sawdust was extracted with hot water to remove ε-galactan and was then partially delignified with acidified sodium chlorite solution. The resulting holocellulose was extracted with 1% and 4% aqueous sodium hydroxide, to give hemicellulose fractions I and II, and with 10% sodium hydroxide to give fraction III (precipitated on acidification of the extract) and fraction IV (precipitated on subsequent addition of acetone). Hydrolysis and chromatography showed the various fractions to be composed of the same sugar residues but in different proportions. Fraction I contained mainly xylan and galactan, fraction II xylan together with appreciable amounts of glucomannan, and fractions III and IV mainly glucomannan with smaller amounts of xylan. Fractions I and II were fractionated by precipitation from water by ammonium sulphate,[3] to give fractions enriched with respect to xylan but still containing galactan or glucomannan.

[1] Campbell, Hirst, and Jones, *J.*, 1948, 774; Jones, *J.*, 1953, 1692; Aspinall, Hirst, and Ramstad, *J.*, 1958, 593.
[2] White, *J. Amer. Chem. Soc.*, 1941, **63**, 2871; 1942, **64**, 302, 1507, 2838; Bouveng and Lindberg, *Acta Chem. Scand.*, 1956, **10**, 1515.
[3] Preece and Mackenzie, *J. Inst. Brewing*, 1952, **58**, 353, 457.

XUM

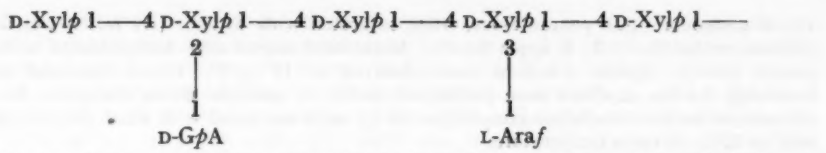
Since hydrolysis of the various hemicellulose fractions gave acidic components in addition to neutral sugars, a quantity of the unfractionated hemicellulose was hydrolysed and the acidic components were separated from the neutral sugars by absorption on an anion-exchange resin. The mixture of neutral sugars contained galactose, glucose, mannose, arabinose, and xylose, together with traces of rhamnose and two other sugars with greater chromatographic mobility. One of the last two sugars was tentatively identified by chromatography as 3-*O*-methylxylose. As far as we are aware this sugar has not previously been found to occur naturally, although the 2-methyl ether has recently been identified as a constituent of plum leaf hemicellulose.[4] The mixture of acidic components was eluted from the anion-exchange resin, and the three main components were separated by chromatography on filter sheets. The first fraction was identified by chromatography and optical rotation as 4-*O*-methyl-D-glucuronic acid. The second fraction was an *O*-(4-*O*-methyl-α-D-glucuronosyl)-D-xylose since the aldobiouronic acid had a high positive rotation ($[\alpha]_D$ +99°) and reduction of the derived methyl ester methyl glycoside with potassium borohydride followed by hydrolysis gave 4-*O*-methyl-D-glucose and D-xylose. The third fraction was probably an aldotriouronic acid since hydrolysis gave the aldobiouronic acid and xylose.

One of the xylan-rich fractions was methylated in the usual way and fractionation of the methylated polysaccharide gave a methylated xylan containing only traces of a methylated hexosan. Hydrolysis of the methylated xylan furnished 2 : 3-di-*O*-methyl-D-xylose and a methylated aldobiouronic acid, together with small amounts of 2 : 3 : 5-tri-*O*-methylarabinose and 2 : 3 : 4-tri-*O*-methyl- and 2- and 3-*O*-methyl-xylose, which were only detected chromatographically. The structure of the methylated aldobiouronic acid was shown by the following experiments to be 3-*O*-methyl-2-*O*-(2 : 3 : 4-tri-*O*-methyl-α-D-glucuronosyl)-D-xylose. The acidic disaccharide was converted into the methyl ester methyl glycoside which was reduced with lithium aluminium hydride. Hydrolysis of part of the partially methylated disaccharide gave 2 : 3 : 4-tri-*O*-methylglucose and 3-*O*-methylxylose. The remaining material was remethylated and hydrolysis of the fully methylated disaccharide gave 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose and 3 : 4-di-*O*-methyl-D-xylose. From the quantities of the major components isolated from the hydrolysis of the methylated polysaccharide it may be concluded that this xylan contains chains of 1 : 4-linked β-D-xylopyranose residues with approximately every fifth xylose residue carrying a terminal 4-*O*-methyl-D-glucuronic acid residue attached as a side-chain to position 2.

In order to obtain more detailed information regarding the fine structure of larch xylans a second series of methylation studies was carried out. The methylated xylan with uronic acid residues present as the sodium salts was readily separated from the methylated polysaccharides without uronic acid residues. The acidic groups were reduced with lithium aluminium hydride, and the reduced methylated xylan was remethylated. Hydrolysis of the methylated reduced xylan afforded 2 : 3 : 4 : 6-tetra- and 2 : 3 : 4-tri-*O*-methyl-D-glucose, 2 : 3 : 5-tri-*O*-methyl-L-arabinose, 2 : 3 : 4-tri-*O*-methyl-, 2 : 3-di-*O*-methyl-, and 2- and 3-*O*-methyl-D-xylose in the approximate molar ratio of 6 : 12 : 5 : 1 : 72 : 20 : 5. The tetra- and tri-*O*-methyl-D-glucose arise from the D-glucuronic acid residues in the xylan, not all tri-*O*-methyl-D-glucose residues being completely remethylated after the reduction. From the previous results it is clear that the 3-*O*-methyl-D-xylose arises from branching points in the main chain to which the uronic acid groups are attached. Since 3-*O*-methyl-D-xylose and the mixture of methyl ethers of D-glucose are present in approximately equimolecular amounts, and since 2-*O*-methyl-D-xylose and 2 : 3 : 5-tri-*O*-methyl-L-arabinose also occur in approximately the same molar proportions, it is probable that the 2-methyl ether arises from branch points to which terminal L-arabofuranose residues are attached. The accompanying partial structure for the xylan indicates the main features of the molecule.

[4] Andrews and Hough, *Chem. and Ind.*, 1956, 1278.

XUM




(D-Xyl*p* = D-xylopyranose, D-G*p*A = 4-*O*-methyl-D-glucuronic acid, and L-Ara*f* = L-arabofuranose)

It is not possible on the present evidence to indicate whether the L-arabofuranose residues are attached directly to the backbone of xylose residues as shown or whether 1 : 4-linked D-xylose residues are interposed with the arabinose residues terminating a longer side-chain. The former alternative is more probable as other xylans (from, *e.g.*, wheat straw [5] and barley husks [6]) are known to contain L-arabofuranose residues directly linked to the backbone of xylose residues.

A molecular-weight determination by the isothermal-distillation method (by the courtesy of Dr. C. T. Greenwood) gave a value of 18,000 ± 500 (degree of polymerisation, 107 ± 3) for the methylated xylan (as methyl ester). This value, taken together with the value of one non-reducing xylose end group per *ca.* 120 sugar residues, suggests that the backbone of xylose residues is unbranched. It is concluded, therefore, that this xylan fraction contains chains of 1 : 4-linked β-D-xylopyranose residues with, on the average, every fifth or sixth residue carrying a terminal 4-*O*-methyl-D-glucuronic acid residue linked through $C_{(2)}$. In addition, a small proportion (*ca.* 4%) of L-arabofuranose residues are present as integral parts of the xylan; these are present as non-reducing end-groups and are probably attached to the backbone through $C_{(3)}$ of xylose residues. In the first methylated xylan fraction, which we examined, the proportion of arabinose residues was very low (<1%) and it is probable that some of the xylan chains carried no arabinose residues. It is clear that in larch wood, as in monocotyledenous plants,[7] several closely related xylans occur side by side.

Several wood xylans have now been examined and all are characterised by the presence of 4-*O*-methyl-D-glucuronic acid residues attached as side-chains to D-xylose by 1 : 2-linkages. The proportions of uronic acid groups are in general somewhat higher in the xylans from soft woods (15—20%) (Western hemlock,[8] Norway spruce,[9] and larch) than in those from hard woods (8—15%) European [10] and North American [11] beech, birch,[12] and aspen [13]). Some of these xylans (Western hemlock, aspen, and larch) also contain a small proportion of L-arabofuranose residues. In contrast, the xylans from cereals [7] are, in general, characterised by a higher proportion of arabinose groups and a lower proportion of uronic acid groups. Despite considerable variations in detailed molecular architecture, however, it is not possible to draw a clear line of demarcation on structural grounds between the xylans from different lignified tissues.

## Experimental

Paper partition chromatography was carried out on Whatman No. 1 and 3MM filter papers with the following solvent systems (v/v): (A) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4); (B) ethyl acetate–pyridine–water (10 : 4 : 3); (C) butan-1-ol–ethanol–water (4 : 1 : 5, upper layer); (D) benzene–ethanol–water (169 : 47 : 15, upper layer); (E) butan-1-ol–acetic acid–water (4 : 1 : 5, upper layer); (F) butan-2-one, saturated with water containing

[5] Bishop, *J. Amer. Chem. Soc.*, 1956, **78**, 2840.
[6] Aspinall and Ferrier, *J.*, 1957, 4188.
[7] Hirst, *J.*, 1955, 2974.
[8] Dutton and Smith, *J. Amer. Chem. Soc.*, 1956, **78**, 2505.
[9] Aspinall and Carter, *J.*, 1956, 3744.
[10] Aspinall, Hirst, and Mahomed, *J.*, 1954, 1734.
[11] Adams, *Canad. J. Chem.*, 1957, **35**, 556.
[12] Saarnio, Wathén, and Gustafsson, *Acta Chem. Scand.*, 1954, **8**, 825.
[13] Jones, Merler, and Wise, *Canad. J. Chem.*, 1957, **35**, 634.

XUM

1% of ammonia; (G) pentan-2-one, 75% saturated with water; (H) butan-1-ol–benzene–pyridine–water (5 : 1 : 3 : 3, upper layer). Methylated sugars were demethylated with hydrobromic acid.[14] Optical rotations were observed at 18° ± 2°. Extractions and reactions involving the use of alkali were performed, as far as possible, under nitrogen. In typical extractions larch holocellulose samples (*ca.* 80 g.) were extracted with alkali (*ca.* 1 l.) in a ball-mill for 12 hr. at room temperature.

*Extraction and Fractionation of Larch Hemicellulose.*—Larch sawdust was extracted successively with boiling benzene and boiling methanol to remove fats and colouring material, and then with water at 90° to remove ε-galactan. The residual sawdust was delignified with acidified sodium chlorite solution according to Wise's procedure.[15] The resulting holocellulose was extracted three times each with 1%, 4%, and 10% sodium hydroxide solutions to give fraction I (6% by weight of the air-dried sawdust), II (4·6%), III (4·0%), and IV (5·0%). Fractions I and II were isolated by acidification of the alkaline extracts with acetic acid (to pH 4—5) and precipitation with an equal volume of acetone. Fraction III was precipitated from the 10% sodium hydroxide extract on acidification, and fraction IV was precipitated on addition of an equal volume of acetone to the supernatant liquid after removal of fraction III. Fraction I, by precipitation from aqueous solution on the stepwise addition of ammonium sulphate, gave a xylan-rich fraction I*a* (precipitated with 50% ammonium sulphate) and galactan-rich fractions I*b* and I*c* (precipitated with 30% and 60% ammonium sulphate). Refractionation of fraction I*a* failed to yield xylan free from galactan. Fraction II was refractionated in a similar way, giving fractions II*a* and II*b* (precipitated with 30 and 50% ammonium sulphate). After five reprecipitations with ammonium sulphate fraction II*b* gave xylan A (1·6%), which was still contaminated with glucomannan. Fraction III was separated into fractions III*a* (1·0%) and III*b* (3·0%), soluble and insoluble in 2% aqueous sodium hydroxide. Fraction III*b* was further separated into fractions III*c* (0·3%), insoluble in 10% sodium hydroxide, III*d* (2·0%), soluble in 10% sodium hydroxide and precipitated on acidification, and III*e* (0·7%), soluble in 10% sodium hydroxide and precipitated, after acidification and removal of III*d*, by the addition of acetone. Fraction IV was separated into fractions IV*a* (4·3%) and IV*b* (0·7%), soluble and insoluble in water.

Chromatography [16] in solvent B of the hydrolysate from xylan A (Found: uronic anhydride, 11·7%) showed xylose (46·5%), mannose + arabinose (18%), glucose (9%), and galactose (3%).

Fraction III*c* (0·5 g.) in acetic anhydride (5 ml.), acetic acid (5 ml.), and concentrated sulphuric acid (0·28 ml.) was kept at room temperature for 7 days. The mixture was poured into ice-water (50 ml.), and the chloroform extract (2 × 25 ml.) was dried and concentrated. The resulting sugar acetates were deacetylated with barium methoxide in methanol and the sugars were examined by chromatography in solvent B. In addition to glucose and traces of mannose, xylose, and galactose, oligosaccharides having the same mobilities as cellobiose and cellotriose were detected. Fraction III*c* was probably a degraded form of cellulose which was extracted together with glucomannan (cf. Aspinall, Laidlaw, and Rashbrook [17]).

Samples of the various hemicellulose fractions were hydrolysed and the relative proportions of the sugars detected on paper chromatograms are indicated in the Table.

*Hydrolysis of Larch Hemicellulose and Examination of the Acidic Components.*—Hemicellulose (fractions I and II; 30 g.) in N-sulphuric acid (700 ml.) was heated on the boiling-water bath for 13·5 hr. (constant rotation). The solution was neutralised with barium hydroxide and barium carbonate, then filtered, and the barium salts were washed with water (3 × 30 ml.). The combined filtrate and washings were freed from barium ions by passage through a column of Amberlite resin IR-120(H) and the acids were adsorbed on a column of Amberlite resin IR-4B (OH). The eluate was concentrated to a syrup (20 g.), and chromatography showed galactose, glucose, mannose, arabinose, and xylose together with traces of rhamnose and two faster-moving sugars. One of the last two sugars was chromatographically similar to 3-*O*-methyl-D-xylose, but distinct from the 2-methyl ether, and gave xylose on demethylation.

The acids were displaced from the resin with N-sulphuric acid, and the eluate was neutralised with barium carbonate, filtered, freed from barium ions with Amberlite resin IR-120(H), and concentrated to a syrup (1·2 g.). Chromatography in solvent A showed three main components

[14] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[15] Wise, *Ind. Eng. Chem. Analyt.*, 1945, **17**, 63.
[16] Flood, Hirst, and Jones, *J.*, 1948, 1679.
[17] Aspinall, Laidlaw, and Rashbrook, *J.*, 1957, 4444.

XUM

having $R_{xylose}$ 1·26, 0·69, and 0·17, and traces of sugars having $R_{xylose}$ 1·60 (probably glucurone) and 0·30. Pure samples of the major acidic sugars were obtained by chromatography on filter sheets with solvent A. Fraction *a* (110 mg.) had $[\alpha]_D$ +83° (*c* 1·1 in $H_2O$) and was chromatographically indistinguishable from 4-*O*-methyl-D-glucuronic acid ($R_{xylose}$ 1·26). Fraction *b* (231 mg.) had $R_{xylose}$ 0·69 and $[\alpha]_D$ +99° (*c* 1·15 in $H_2O$). The acid was converted into the methyl ester methyl glycoside (185 mg.) which was treated with potassium borohydride (400 mg.) in water (10 ml.) for 18 hr. Excess of hydride was destroyed by the addition of acetic

| Hemicellulose fraction | Method of isolation | Paper chromatography: Man | Glu | Gal | A | Xyl | UA |
|---|---|---|---|---|---|---|---|
| I | Extrn. with 1% NaOH | + | + | +++ | ++ | +++ | ++ |
| I*a* | Ammonium sulphate | + | + | + | + | +++ | ++ |
| I*b* and I*c* | Pptn. | — | — | +++ | ++ | + | tr |
| II | Extrn. with 4% NaOH | ++ | + | + | + | +++ | ++ |
| II*a* | Ammonium sulphate | +++ | ++ | + | tr | +++ | ++ |
| II*b* | Pptn. | ++ | + | + | tr | +++ | ++ |
| III | Extrn. with 10% NaOH | +++ | ++ | + | — | ++ | + |
| III*a* | Sol. in 2% NaOH | +++ | ++ | + | — | +++ | ++ |
| III*b* | Insol. in 2% NaOH | +++ | ++ | + | — | + | tr |
| III*c* | Insol. in 10% NaOH | tr | +++ | tr | — | tr | — |
| III*d* | Sol. in 10% NaOH | +++ | ++ | tr | — | tr | — |
| III*e* | Sol. in 10% NaOH | +++ | ++ | + | — | + | tr |
| IV | Extrn. with 10% NaOH | +++ | ++ | + | — | ++ | + |
| IV*a* | Sol. in $H_2O$ ..... | +++ | ++ | + | — | +++ | ++ |
| IV*b* | Insol. in $H_2O$ | +++ | ++ | + | — | + | tr |

(Man = mannose, Glu = glucose, Gal = galactose, A = arabinose, Xyl = xylose, and UA = uronic acid. tr = trace.)

acid, and the solution was de-ionised by passage through columns of Amberlite resins IR-120(H) and IR-4B(OH) and concentrated to a syrup (140 mg.). The syrup (135 mg.) was hydrolysed with 0·8N-sulphuric acid (5 ml.) at 100° for 5 hr. After neutralisation with barium carbonate the resulting syrup (106 mg.) was separated on filter sheets with solvent H, to give fractions *d* (43 mg.) and *e* (35 mg.). Fraction *d* had $[\alpha]_D$ +54° (*c* 0·85 in $H_2O$) and was identified as 4-*O*-methyl-D-glucose by conversion into the phenylosazone, m. p. 149—152°, characterised by circular paper chromatography and by *X*-ray powder photography. Fraction *e* had $[\alpha]_D$ +20° (*c* 0·70 in $H_2O$) and was identified as D-xylose by conversion into the di-*O*-benzylidene dimethyl acetal, m. p. and mixed m. p. 210°. The acid fraction *c* (150 mg.) had $R_{xylose}$ 0·17 and on hydrolysis gave xylose and the aldobiouronic acid having $R_{xylose}$ 0·69.

*Preparation of Methylated Xylan A, Hydrolysis, and Separation of Methylated Sugars.*— Xylan A (10 g.) was methylated by successive additions of methyl sulphate and sodium hydroxide, and then with methyl iodide and silver oxide to give methylated polysaccharide (3·5 g.), $[\alpha]_D$ −51·5° (*c* 0·34 in $CHCl_3$) (Found: OMe, 40·1%). A sample of this material was hydrolysed and chromatography of the hydrolysate showed methylated hexoses in addition to methylated pentoses and acidic components. The methylated polysaccharide was fractionated by dissolution in boiling chloroform–light petroleum (b. p. 60—65°) mixtures and three main fractions were obtained, (1) [0·40 g., soluble in chloroform–light petroleum (1 : 4); OMe, 45·0%], (2) [0·95 g., soluble in chloroform–light petroleum (1 : 3); OMe, 38·5%], and (3) [1·0 g., soluble in chloroform–light petroleum (3 : 7); OMe, 37·9%]. Samples of these fractions were hydrolysed and the hydrolysates were examined chromatographically, fraction 1 giving methylated hexoses and traces of methylated pentoses, and fractions 2 and 3 giving methylated pentoses together with acidic components and traces of methylated hexosis. Fractions 2 and 3 were combined, dissolved in chloroform, and precipitated by light petroleum, to give methylated xylan A (1·8 g.), $[\alpha]_D$ −61° (*c* 0·23 in $CHCl_3$) (Found: OMe, 38·1%).

Methylated xylan A (1·5 g.) was hydrolysed successively with boiling methanolic 5% hydrogen chloride (170 ml.) for 8 hr. and with 0·5N-hydrochloric acid (100 ml.) at 100° for 12·5 hr. The cooled solution was neutralised with silver carbonate, hydrogen sulphide was passed through the filtrate to precipitate silver salts, and the solution was concentrated to a syrup. The syrup was dissolved in water, the acidic components were converted into barium salts by treatment with barium carbonate, and the solution was taken to dryness. The resulting syrup was extracted with chloroform to give syrup A (1·01 g.) and an insoluble residue, which was dissolved in water, passed through a column of Amberlite resin IR-100(H) to remove barium ions, and concentrated to give acidic fraction B (139 mg.).

XUM

Syrup A (1·01 g.) was fractionated on cellulose (40 × 3 cm.) with light petroleum (b. p. 100—120°)–butan-1-ol (7 : 3; later, 1 : 1) saturated with water, and butan-1-ol half saturated with water as eluants, to give six fractions. Fractions 1—3 contained only neutral sugars. Fractions 4 and 6 contained only acidic components; these were combined and after removal of barium ions with Amberlite resin IR-100(H) gave acidic fraction C (116 mg.). Fraction 5 contained neutral and acidic sugars.

*Examination of Neutral Sugars.*—Chromatography of fraction 1 (26·5 mg.) in solvent C showed only one component ($R_G$ 0·95). Since the syrup did not crystallise a small sample was rehydrolysed and a second component ($R_G$ 0·73 in solvent C) was observed. The remainder of the syrup was rehydrolysed and chromatography in solvent D showed three sugars, 2 : 3 : 5-tri-*O*-methylarabinose, 2 : 3 : 4-tri-*O*-methylxylose, and 2 : 3-di-*O*-methylxylose. The proportions of the sugars were estimated by Pridham's method,[18] and the result indicated the presence in the original syrup of tri-*O*-methylxylose (10 mg.), tri-*O*-methylarabinose (5·5 mg.), and methyl di-*O*-methylxyloside (11 mg.). Fraction 2 (20 mg.) contained tri-*O*-methylhexose ($R_G$ *ca.* 0·80 in solvent C) and on demethylation gave mannose, glucose, and a trace of galactose. Fraction 3 (404 mg.) crystallised on being seeded with 2 : 3-di-*O*-methyl-β-D-xylose and had m. p. 78° and $[\alpha]_D$ +23° (equil.) (*c* 0·82 in $H_2O$) (Found: OMe, 35·1. Calc. for $C_7H_{14}O_5$: OMe, 34·8%). The identity of the sugar was confirmed by conversion into 2 : 3-di-*O*-methyl-*N*-phenyl-D-xylosylamine, m. p. and mixed m. p. 122—123°, and into 2 : 3-di-*O*-methyl-D-xylonamide, m. p. 132°. Fraction 5 (32 mg.) contained mono-*O*-methylxylose and a small amount of an acidic component and had $[\alpha]_D$ +44° (*c* 1·43 in $H_2O$). The neutral sugars (28 mg.) were separated from the acid on a filter sheet by using solvent C, and paper ionophoresis showed 2- and some 3-*O*-methylxylose. The syrupy mixture of methyl pyranosides, prepared by refluxing the sugars with dry methanolic hydrogen chloide, consumed 0·20 mol. of periodate (spectrophotometric determination [19] carried out by Dr. R. J. Ferrier), showing that the 2- and the 3-methyl ether were present in the ratio of 1 : 4.

*Examination of the Acidic Fractions.*—Chromatography of acidic fractions B and C in solvent E showed both to contain a main component and a second component moving slightly more slowly. On vigorous hydrolysis both fractions gave 2 : 3 : 4-tri-*O*-methylglucuronic acid, mono-*O*-methylxylose, and a trace of 2 : 3-di-*O*-methylxylose. Fraction C (95 mg.) was refluxed with methanolic 1% hydrogen chloride (15 ml.) for 6 hr. The product, after neutralisation with silver carbonate, was dissolved in methylal (15 ml.), lithium aluminium hydride (100 mg.) was added, and the solution was refluxed for 2 hr. Excess of hydride was destroyed by water, and the methylal layer was separated and concentrated. The aqueous layer was taken to dryness and the residue was extracted with acetone. The solid residue was suspended in water (25 ml.), shaken with Amberlite resin IR-100(H), taken to dryness, and extracted again with acetone. The combined extracts (70 mg.) were hydrolysed with 0·8N-hydrochloric acid (14 ml.) at 100° for 6 hr., and the hydrolysate (45 mg.) was separated on a filter sheet by using solvent E, to give fractions *a* (19 mg.) and *b* (7 mg.). Fraction *a* had $[\alpha]_D$ +50° (±3°) and was chromatographically identical with 2 : 3 : 4-tri-*O*-methyl-D-glucose. Fraction *b* was chromatographically and ionophoretically indistinguishable from 3-*O*-methyl-D-xylose and gave xylose on demethylation. Acidic fraction B (125 mg.), after conversion into methyl ester methyl glycoside, was reduced in a similar way, and the product was methylated with methyl iodide and silver oxide. The fully methylated disaccharide (95 mg.) was hydrolysed with 0·8N-hydrochloric acid (15 ml.) at 100° for 6 hr., and the hydrolysis products were separated on filter sheets with solvent E to give fractions *c* (53 mg.) and *d* (33 mg.). Fraction *c* had $[\alpha]_D$ +80° (±2°) and was identified as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose by conversion into the aniline derivative, m. p. and mixed m. p. 135—137°. Chromatography and ionophoresis of fraction *d* showed only 3 : 4-di-*O*-methylxylose, and the sugar was characterised by conversion into 3 : 4-di-*O*-methyl-D-xylonolactone, m. p. and mixed m. p. 65·5—66·5°.

*Preparation of Methylated Reduced Xylan B.*—Larch hemicellulose (fraction II; 20 g.) was methylated with methyl sulphate and sodium hydroxide, and the crude methylated polysaccharide which was isolated was separated into fractions C and D, respectively soluble and insoluble in acetone. The insoluble residue (D) was dispersed in acetone–water (1 : 1), further acetone (3 vol.) was added, inorganic salts, which separated, were filtered off, the filtrate was taken to dryness, and the residue was separated into fractions E and F, respectively soluble and

[18] Pridham, *Analyt. Chem.*, 1956, **28**, 1967.
[19] Aspinall and Ferrier, *Chem. and Ind.*, 1957, 1216.

insoluble in boiling chloroform. Fractions C and E were combined, dissolved in chloroform, and precipitated by the addition of light petroleum. This precipitate (7·5 g.) was probably a mixture of methylated glucomannan and methylated xylan (in the acid form) since chromatography of the hydrolysate showed methylated hexoses, methylated pentoses, and acidic components. The chloroform-insoluble residue (F) was dispersed in ethanol–water (9 : 1), and addition of ether precipitated methylated xylan B (12·0 g.; as sodium salt). Chromatography of the hydrolysate showed methylated pentoses together with acidic components, but no methylated hexoses. Methylated xylan B (11·9 g.; as sodium salt) in acetone–water (400 ml., 1 : 1) was shaken with Amberlite resin IR-120(H) for 30 min., further acetone (200 ml.) being added to maintain solution. Acetone was removed from the filtrate under reduced pressure at 15°, the aqueous dispersion was extracted with chloroform, and the dried extract was concentrated and poured into light petroleum to give methylated xylan B (7·9 g., as free acid). The methylated xylan acid (7·9 g.) was treated with methyl iodide and silver oxide, giving the methylated xylan methyl ester (7·3 g.), $[\alpha]_D$ −52° (*c* 0·89 in $CHCl_3$) (Found: OMe, 39·3%). The methylated polysaccharide (7·1 g.) in refluxing tetrahydrofuran (330 ml.) was reduced by lithium aluminium hydride (1·4 g.) for 3 hr. After destruction of excess of hydride by water the mixture was taken to dryness and the methylated polysaccharide was isolated by extraction with acetone. After a second reduction with lithium aluminium hydride, the product was remethylated with methyl iodide and silver oxide, to give methylated reduced xylan B (5·2 g.), $[\alpha]_D$ −52° (*c* 0·40 in $CHCl_3$) (Found: OMe, 37·2%).

*Hydrolysis of Methylated Reduced Xylan B and Separation of Methylated Sugars.*—0·5N-Hydrochloric acid was added slowly to methylated reduced xylan B (4·5 g.) in boiling methanol (300 ml.). The rates of addition of acid and of distillation of methanol were adjusted so that complete solution was maintained, acid (650 ml.) being added during 10 hr. while 630 ml. of distillate were collected. Water (100 ml.) was added and the solution (N with respect to hydrochloric acid) was heated at 100° for 4 hr. (constant rotation). The cooled solution was neutralised with silver carbonate and concentrated to a syrup (4·8 g.) which was fractionated on cellulose (70 × 5 cm.) with light petroleum (b. p. 100—120°)–butan-1-ol (7 : 3) saturated with water, and butan-1-ol half saturated with water as eluants, to give four fractions.

*Fraction* 1. Chromatography of the syrup (500 mg.) in solvents D and G showed 2 : 3 : 4 : 6-tetra-*O*-methylglucose, 2 : 3 : 5-tri-*O*-methylarabinose, and 2 : 3 : 4-tri-*O*-methylxylose. Since hydrolysis of a sample gave small amounts of di- and mono-*O*-methylxylose (presumably derived from methyl glycosides) the syrup (*ca.* 480 mg.) was rehydrolysed with 0·5N-hydrochloric acid (50 ml.) at 100° for 5 hr., and the hydrolysate (433 mg.) was refractionated on cellulose (80 × 2 cm.) with the same solvents, to give six fractions. Fraction 1*a* (23 mg.) had m. p. 72—75° and $[\alpha]_D$ +81° (equil.) (*c* 0·45 in $H_2O$) and was identified as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose by conversion into the aniline derivative, m. p. and mixed m. p. 134—135°. Fraction 1*b* (178 mg.) contained 2 : 3 : 4 : 6-tetra-*O*-methylglucose and 2 : 3 : 5-tri-*O*-methylarabinose in the ratio of 0·73 : 1 (estimated by Pridham's method [18]). A sample (42 mg.) of 2 : 3 : 5-tri-*O*-methyl-L-arabinose, $[\alpha]_D$ −29° (*c* 0·42 in $H_2O$), was separated on filter sheets with solvent G and identified by conversion into 2 : 3 : 5-tri-*O*-methyl-L-arabonamide, m. p. 137—138°. Fraction 1*c* (27 mg.), $[\alpha]_D$ +19° (*c* 0·27 in $H_2O$), was chromatographically indistinguishable from 2 : 3 : 4-tri-*O*-methyl-D-xylose but attempts to prepare the aniline derivative failed. Fractions 1*d* (9 mg.), 1*e* (15 mg.), and 1*f* (9 mg.) were shown by chromatography to contain 2 : 3 : 4-tri-*O*-methylglucose, and 2 : 3-di- and mono-*O*-methylxylose respectively.

*Fraction* 2. The chromatographically pure syrup (492 mg.) (Found: OMe, 41·8. Calc. for $C_9H_{18}O_6$: OMe, 41·9%) had $[\alpha]_D$ +67° (*c* 0·82 in $H_2O$) and was identified as 2 : 3 : 4-tri-*O*-methyl-D-glucose by conversion into the aniline derivative, m. p. and mixed m. p. 144—145°.

*Fraction* 3. The sugar (2·325 g.) crystallised when seeded with 2 : 3-di-*O*-methyl-β-D-xylose and had m. p. 70—75° (Found: OMe, 34·5. Calc. for $C_7H_{14}O_5$: OMe, 34·9%). The sugar was identified by conversion into 2 : 3-di-*O*-methyl-D-xylonamide, m. p. and mixed m. p. 130—132°.

*Fraction* 4. Chromatography (solvent F) and ionophoresis of the syrup (730 mg.) disclosed 2- and 3-*O*-methylxylose. The optical rotation {$[\alpha]_D$ +23·0° (*c* 1·46 in $H_2O$)} of the syrup corresponded to that of a mixture of 2-*O*-methyl-D-xylose [20] ($[\alpha]_D$ +35·9°) and 3-*O*-methyl-D-xylose [19] ($[\alpha]_D$ +19·5°) in the ratio of 1 : 4. The periodate consumed (0·19 mol.) (spectrophotometric determination [19]) by the derived syrupy mixture of methyl pyranosides indicated that 19% of the 2-methyl ether was present in the mixture. The syrup (500 mg.) was

[20] Robertson and Speedie, *J.*, 1934, 824.

refractionated on cellulose (40 × 3 cm.) with solvent R, to give three fractions. Fraction 4*a* (312 mg.), $[\alpha]_D$ +19° (*c* 0·69 in $H_2O$), was chromatographically and ionophoretically pure, and was identified as 3-*O*-methyl-D-xylose by conversion into the phenylosazone, m. p. and mixed m. p. 170—171°. Fraction 4*b* (45 mg.) contained mainly 3-*O*-methylxylose with small amounts of the 2-methyl ether. Fraction 4*c* (89 mg.), $[\alpha]_D$ +33° (*c* 0·36 in $H_2O$), contained mainly the 2-methyl ether with small amounts of the 3-methyl ether. 2-*O*-Methyl-D-xylose was identified by conversion into the aniline derivative, m. p. and mixed m. p. 125—126°.

The authors thank Professor E. L. Hirst, F.R.S., for his interest and advice, Messrs. Alex Cowan and Sons Ltd. for financial assistance (to J. E. McK.), and the Rockefeller Foundation for a grant.

DEPARTMENT OF CHEMISTRY, UNIVERSITY OF EDINBURGH. [*Received, October* 31*st*, 1957.]

---

## 212. *Alicyclic Glycols. Part XIV.* The Tetralin-2 : 3-diols and the* cyclo*Hex-4-ene-1 : 2-diols.*

By MD. ERFAN ALI and L. N. OWEN.

New syntheses of three of these diols are described. The infrared spectra show the presence of intramolecular hydrogen bonding in all four. The rates of reaction of the monotoluene-*p*-sulphonates with alkali, and the rates of oxidation of the tetralin-2 : 3-diols with lead tetra-acetate, are higher than for the corresponding stereoisomers of *cyclo*hexane-1 : 2-diol, probably because of less hindrance by axially disposed hydrogen atoms. The results indicate that the *cyclo*hexene ring in both sets of compounds is in the half-chair conformation.

IN contrast to the extensive information which is now available on the relation between stereochemistry and reactivity in *cyclo*hexane systems, comparatively little is known about the *cyclo*hexene analogues. The preferred conformation [1,2] of *cyclo*hexene itself is the " half-chair " form (I) [or the alternative half-chair with which (I) is interconvertible] in which only the valencies at $C_{(4)}$ and $C_{(5)}$ are in the normal axial and equatorial positions, those at $C_{(3)}$ and $C_{(6)}$ being termed " quasi-axial " and " quasi-equatorial." Similar considerations have been applied [2,3] to the tetralin system in the classical fixed-bonded structure (II), although the bond common to both rings is not of course identical with the ordinary double bond in *cyclo*hexene. The present paper is concerned with the stereoisomers of tetralin-2 : 3-diol and of *cyclo*hex-4-ene-1 : 2-diol; in the half-chair conformations, the hydroxyl groups in these compounds would all be in true axial or equatorial positions.

Tetralin-*trans*-2 : 3-diol can be readily obtained [4,5] by hydrolysis of 2 : 3-dibromotetralin, or by hydration of 2 : 3-epoxytetralin,but no convenient preparation of the *cis*-isomer has been reported. Leroux [5] obtained a mixture of stereoisomers by reaction of the same dibromide with silver acetate in acetic acid (which was probably [6] not anhydrous) followed by hydrolysis of the resulting diacetates, and by fractional crystallisation he separated the *cis*-diol from a molecular compound of the *cis*- and *trans*-forms; later workers [7] effected a separation by formation of the *iso*propylidene derivative of the *cis*-diol. The configurations assigned in the early work were erroneous, being based on

* Part XIII, Owen and Peto, *J.*, 1955, 2383.

[1] Beckett, Freeman, and Pitzer, *J. Amer. Chem. Soc.*, 1948, **70**, 4227; Raphael and Stenlake, *Chem. and Ind.*, 1953, 1286.
[2] Barton, Cookson, Klyne, and Shoppee, *ibid.*, 1954, 21.
[3] Lasheen, *Acta Cryst.*, 1952, **5**, 593; cf. Mosettig and Scheer, *J. Org. Chem.*, 1952, **17**, 764.
[4] Bamberger and Lodter, *Ber.*, 1893, **26**, 1833; *Annalen*, 1895, **288**, 74.
[5] Leroux, *Ann. Chim.* (*France*), 1910, **21**, 458.
[6] Cf. Winstein and Buckles, *J. Amer. Chem. Soc.*, 1942, **64**, 2787.
[7] Böeseken and Derx, *Rec. Trav. chim.*, 1921, **40**, 519.

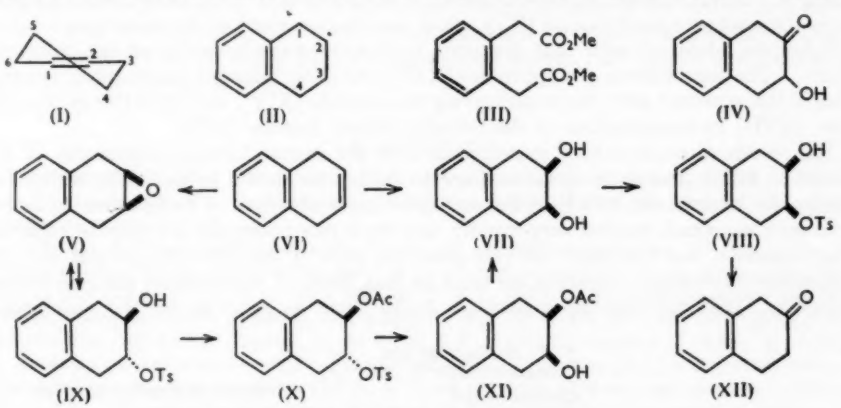
XUM

the assumption of *cis*-opening of an epoxide ring, but they were corrected by Böeseken and Derx; [7] rigid confirmation has recently been provided [8] by resolution of the *trans*-diol.

Hydroxylation of a *cyclo*alkene with buffered aqueous permanganate has been successfully used for the preparation of *cis*-diols in the *cyclo*pentene,[9] *cyclo*hexene,[10] and *cyclo*heptene [11] series, and we therefore applied the method to 1 : 4-dihydronaphthalene (VI) but the yield of tetralin-*cis*-2 : 3-diol (VII) was very low, and only slightly better results were obtained by the use of sodium chlorate–osmium tetroxide. Woodward's method [12] (silver acetate and iodine in wet acetic acid) gave, however, the *cis*-diol in 60% yield. The poor results from the first two methods were probably due to the low solubility of the hydrocarbon in the reaction media. An alternative route to the *cis*-diol, *via* the *trans*-monotoluene-*p*-sulphonate, is described below.

As a possible new approach to the tetralin-2 : 3-diols, the acyloin cyclisation of dimethyl *o*-phenylenediacetate (III) by sodium and liquid ammonia [13] was investigated, but instead of the expected ketol (IV) the only identifiable product was naphthalene-2 : 3-diol, possibly formed by disproportionation of the ketol.

Monoesters of tetralin-*trans*-2 : 3-diol were prepared by reaction of 2 : 3-epoxytetralin (V) with acetic, toluene-*p*-sulphonic, and methanesulphonic acid, which gave the *trans*-monoesters, *e.g.*, (IX). These were characterised as the following simple and mixed diesters: *trans*-acetate toluene-*p*-sulphonate (X) (obtained from the monoacetate and from the monotoluene-*p*-sulphonate), *trans*-ditoluene-*p*-sulphonate, *trans*-methanesulphonate toluene-*p*-sulphonate, *trans*-benzoate toluene-*p*-sulphonate, *trans*-dimethanesulphonate, *trans*-acetate methanesulphonate. The *cis*-monoacetate (XI) was prepared in good yield by reaction of either the *trans*-acetate toluene-*p*-sulphonate (X) or the *trans*-acetate methanesulphonate with aqueous acetone in the presence of calcium carbonate

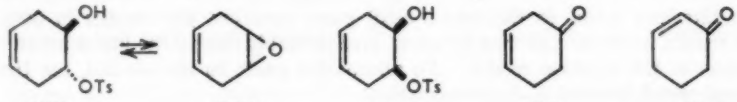



(Ts = *p*-$C_6H_4Me\cdot SO_2$)

(cf. ref. 11), and the configuration of the product was confirmed by deacetylation to the *cis*-diol (VII). Reaction of the *cis*-monoacetate with toluene-*p*-sulphonyl chloride in pyridine gave the *cis*-acetate toluene-*p*-sulphonate; attempts to prepare the *cis*-monotoluene-*p*-sulphonate (VIII) by preferential alcoholysis of the acetyl group in this derivative were not successful, but it was obtained by direct esterification of the *cis*-diol under controlled conditions, and was characterised as the *cis*-ditoluene-*p*-sulphonate and the *cis*-acetate toluene-*p*-sulphonate.

[8] Lettré and Lerch, *Chem. Ber.*, 1952, **85**, 394.
[9] Owen and Smith, *J.*, 1952, 4026.
[10] Clarke and Owen, *J.*, 1949, 315.
[11] Owen and Saharia, *J.*, 1953, 2582.
[12] Cf. Ginsburg, *J. Amer. Chem. Soc.*, 1953, **75**, 5746.
[13] Cf. Sheehan and Coderre, *ibid.*, p. 3997.

The monosulphonates of tetralin-2 : 3-diol behaved qualitatively towards alkali as did the corresponding derivatives of *cyclo*pentane-,[9] *cyclo*hexane-,[10] and *cyclo*heptane-1 : 2-diol.[11] Thus, the *trans*-monotoluene-*p*-sulphonate (IX) and the *trans*-monomethanesulphonate gave the epoxide (V) whilst the *cis*-monotoluene-*p*-sulphonate (VIII) and the *cis*-acetate toluene-*p*-sulphonate gave β-tetralone (XII). The rates of these reactions are discussed later.




(XIII) (XIV) (XV) (XVI) (XVII)

Reaction of *trans*-monotoluene-*p*-sulphonate (IX) with lithium chloride resulted in the expected [11] overall retention of configuration (two successive inversions) and gave *trans*-3-chlorotetralin-2-ol. In a similar reaction the *cis*-monotoluene-*p*-sulphonate gave a ketonic product, probably mainly β-tetralone.

Syntheses of both forms of *cyclo*hex-4-ene-1 : 2-diol have recently been described, the *cis*-isomer being obtained [14] by Diels–Alder reaction of vinylene carbonate with butadiene, and the *trans*-form by controlled hydroxylation of *cyclo*hexa-1 : 4-diene with silver benzoate and iodine.[15] Different methods were used in the present work. The *trans*-diol was prepared by hydration of 4 : 5-epoxy*cyclo*hexene (XIV), and the *cis*-isomer from the same source *via* the *trans*-monotoluene-*p*-sulphonate (XIII), *trans*-acetate toluene-*p*-sulphonate, and *cis*-monoacetate, as described above in the tetralin series; yields were excellent at all stages. Direct monotoluene-*p*-sulphonation of the *cis*-diol under mild conditions gave the *cis*-monotoluene-*p*-sulphonate (XV), which was characterised as the *cis*-acetate toluene-*p*-sulphonate, identical with that prepared by toluene-*p*-sulphonation of the *cis*-monoacetate. The monotoluene-*p*-sulphonates (XIII) and (XV) behaved qualitatively towards alkali in the expected way, the former giving the epoxide (XIV), and the latter *cyclo*hex-2-enone (XVII) by isomerisation of the initially formed 3-enone (XVI).

The results of reaction-rate measurements on the monotoluene-*p*-sulphonates of the tetralin-2 : 3-diols and of the *cyclo*hex-4-ene-1 : 2-diols are shown in the Table, which also includes, for comparison, data [11] on the corresponding derivatives of *cyclo*hexane-1 : 2-diol. The *trans*-compounds reacted very rapidly, and their rate constants can only be regarded as approximate, but the *trans* : *cis* rate-ratio, *ca.* 4000 : 1 for both the tetralin and the *cyclo*hexene derivatives, is roughly the same as that, 3000 : 1, observed for the *cyclo*hexane analogues. That the absolute values are 5—10 times as great as for the *cyclo*hexane

| | Bimolecular rate constant (mole$^{-1}$ l. min.$^{-1}$) | | Infrared absorption max. (cm.$^{-1}$) | | |
|---|---|---|---|---|---|
| | Alkaline hydrol. of monotoluene-*p*-sulphonate | $Pb(OAc)_4$ oxidn. | Free OH | Bonded OH | $\Delta\nu$ |
| Tetralin-*cis*-2 : 3-diol ..... | 0·037 | 14·8 | 3622 | 3590 | 32 |
| Tetralin-*trans*-2 : 3-diol ..... | *ca.* 150 | 1·52 | 3630 | 3598 | 32 |
| *cyclo*Hex-4-ene-*cis*-1 : 2-diol | 0·023 | — | 3622 | 3590 | 32 |
| *cyclo*Hex-4-ene-*trans*-1 : 2-diol | *ca.* 100 | — | 3630 | 3595 | 35 |
| *cyclo*Hexane-*cis*-1 : 2-diol ... | 0·005 * | 8·1 † | 3626 | 3587 | 39 ‡ |
| *cyclo*Hexane-*trans*-1 : 2-diol | 15 * | 0·33 | 3634 | 3602 | 32 ‡ |

* Ref. 11. † Ref. 17. ‡ Ref. 19.

compound of corresponding configuration can probably be attributed to the absence of axial hydrogen atoms at the ends of the alicyclic double bond; consequently there will be less steric hindrance to the attainment by the toluene-*p*-sulphonyloxy-group (and also

[14] Newman and Addor, *J. Amer. Chem. Soc.*, 1955, **77**, 3789.
[15] McCasland and Horswill, *ibid.*, 1954, **76**, 1654.

XUM

by the hydroxyl group in the *trans*-compounds) of the axial position which is required, both with the *cis*- and the *trans*-compounds, for the energetically favoured planar four-centre displacement mechanism[16] (*i.e.*, toluene-*p*-sulphonyloxy-group and neighbouring hydrogen both axial for ketone formation, toluene-*p*-sulphonyloxy-group and neighbouring hydroxyl both axial for epoxide formation).

Oxidations of the *cyclo*hex-4-ene-1 : 2-diols with lead tetra-acetate were not attempted, because of the complications arising from the presence of the double bond, but rate measurements were made at 25° on the two tetralin-2 : 3-diols (see Table). The *cis* : *trans* rate-ratio is of the same order as for the *cyclo*hexane-1 : 2-diols, and very much smaller than would be expected for a boat conformation of the *cyclo*hexene ring; in the latter form, the *cis*-diol should exhibit reactivity of a much higher order of magnitude.[17] The somewhat higher values for the tetralin-2 : 3-diols than for the corresponding *cyclo*hexane compounds may again be due to decreased steric hindrance, particularly with the *trans*-isomer where crowding of the axial hydrogen atoms in the *cyclo*hexane system tends to resist the attainment by the two C–OH bonds of the closer approach to co-planarity which would facilitate formation of the supposed[18] cyclic transition state.

Confirmatory evidence for the half-chair conformation of the tetralin- and the *cyclo*hexene-diols was provided by their infrared spectra (see Table). Dilute solutions in carbon tetrachloride showed in all four cases absorption maxima of the type which Kuhn[19] has shown to be characteristic of the presence of both free and intramolecularly bonded hydroxyl groups, the relative intensities of the two peaks being independent of concentration. The separations of the bands, $\Delta\nu$, show good agreement with those reported for the *cyclo*hexane-1 : 2-diols, there being no significant difference between the *cis*- and the *trans*-forms. This indicates[19] that the distance between the hydroxyl groups in each stereoisomer is the same, a condition which can be satisfied only in the half-chair conformation. This conformation is of course itself stabilised by the intramolecular hydrogen bonding, and it does not follow from the above observations that tetralin and *cyclo*hexene necessarily exist in the same form.

## Experimental

Analyses were by Miss J. Cuckney and her staff, and absorption spectra by Mr. R. L. Erskine, B.Sc., A.R.C.S., and Mrs. A. I. Boston. A calcium fluoride prism was used for the infrared absorption measurements.

*Dimethyl* o-*Phenylenediacetate*.—Treatment of ωω′-dicyano-*o*-xylene (19 g.) with 50% sulphuric acid (340 g.) under reflux for 2 hr., followed by cooling in ice, gave *o*-phenylenediacetic acid (22 g., 93%), m. p. 151—152° (lit.,[20] m. p. 150°). Esterification by the azeotropic method, using methanol, benzene, and sulphuric acid, gave the *dimethyl* ester (86%), b. p. 110°/0·2 mm., $n_D^{21}$ 1·5120 (Found: C, 64·8; H, 6·5. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%).

*Acyloin Cyclisation of Dimethyl* o-*Phenylenediacetate*.—The ester (2 g.) in dry ether (180 c.c.) was added to a solution of sodium (1·6 g.) in liquid ammonia (300 c.c.) and dry ether (200 c.c.) during 2 hr. Evaporation to dryness, followed by decomposition of the excess of sodium with dry methanol (4 c.c.) in dry ether (30 c.c.), afforded a yellow residue which was acidified with acetic acid (5 g.) in dry ether (70 c.c.), and then diluted with water. The ether layer was washed successively with water, aqueous sodium hydrogen carbonate, again with water, and then dried ($Na_2SO_4$). Removal of the solvent gave a semi-solid residue which on recrystallisation from benzene gave naphthalene-2 : 3-diol (0·3 g., 21%), m. p. and mixed m. p. 163—164°.

*Tetralin*-trans-2 : 3-*diol*.—2 : 3-Epoxytetralin,[21] on hydration with aqueous acetic acid,[4,5] gave the *trans*-diol, m. p. 135—136°. Infrared absorption: see Table. Treatment of the diol with a slight excess of the appropriate acid chloride in pyridine for 12 hr. at room temperature

[16] Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44.
[17] Eliel and Pillar, *J. Amer. Chem. Soc.*, 1955, **77**, 3600; and references there cited.
[18] Cf. Waters, *J.*, 1956, 840.
[19] Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492; 1954, **76**, 4323.
[20] Moore and Thorpe, *J.*, 1908, **93**, 175.
[21] Cook and Hill, *J. Amer. Chem. Soc.*, 1940. **62**, 1995.

XUM

gave the *trans*-ditoluene-*p*-sulphonate, plates (from methanol), m. p. 143—144° (Found: C, 60·9; H, 5·2; S, 13·45. Calc. for $C_{24}H_{24}O_6S_2$: C, 61·0; H, 5·1; S, 13·6%) (lit.,[22] m. p. 140—141°); and the trans-*dimethanesulphonate*, needles (from methanol), m. p. 141° (Found: C, 45·2; H, 5·1; S, 19·6. $C_{12}H_{16}O_6S_2$ requires C, 45·0; H, 5·0; S, 20·0%).

*Tetralin*-cis-2 : 3-*diol*.—(i) A solution of potassium permanganate (7·8 g.) and magnesium sulphate (12·2 g.; hydrated) in water (365 c.c.) was added to a vigorously stirred suspension of 1 : 4-dihydronaphthalene [21] (8 g.; purified through the mercuric acetate addition compound[23]) in ethanol (150 c.c.) at *ca.* −15° during 2 hr. The mixture was left overnight at room temperature, then filtered, and the solution was saturated with sodium chloride and continuously extracted with ether to give a solid, which on repeated crystallisation, first from benzene and then from water, gave the *cis*-diol (0·21 g., 2%), m. p. 124° (lit.,[24] m. p. 124—125°).

(ii) 1 : 4-Dihydronaphthalene (8 g.) and a solution of sodium chlorate (17 g.) in water (200 c.c.) containing osmium tetroxide (0·1 g.) were vigorously stirred together for 24 hr. at 50°; there was still a strong characteristic odour of 1 : 4-dihydronaphthalene. The mixture was then cooled, made alkaline with 10% aqueous sodium hydroxide, washed with a little ether to remove the unchanged hydrocarbon, and then continuously extracted with ether to give tetralin-*cis*-2 : 3-diol (1·1 g., 11%), m. p. 123—124° (from water).

(iii) To a stirred mixture of 1 : 4-dihydronaphthalene (6 g.), acetic acid (380 c.c.), water (1 c.c.), and silver acetate (16 g.), iodine (11 g.) was added in small portions during 30 min. The mixture was stirred for a further 3 hr. at room temperature, and for 3 hr. at 100°; it was then filtered and evaporated to dryness. The residue was dissolved in methanol (300 c.c.), treated with excess of potassium hydroxide (5 g. after neutralisation), and set aside overnight. The solution was then neutralised with acetic acid, and evaporated, with addition of water, to remove methanol. Continuous ether-extraction of the residual aqueous solution gave the *cis*-diol (4·5 g., 59%), m. p. 124° (from water). Infrared absorption: see Table.

Treatment of the *cis*-diol with toluene-*p*-sulphonyl chloride (2·1 mol.) in pyridine gave the cis-*ditoluene*-p-*sulphonate*, plates (from methanol), m. p. 124° (Found: C, 60·75; H, 5·3; S, 13·4. $C_{24}H_{24}O_6S_2$ requires C, 61·0; H, 5·1; S, 13·6%).

*Monoacetate of Tetralin*-trans-2 : 3-*diol*.—2 : 3-Epoxytetralin (1 g.) in acetic acid (5 c.c.) was heated on the steam-bath for 20 hr. Removal of most of the excess of acid under reduced pressure, followed by dissolution of the residue in ether, washing with aqueous sodium hydrogen carbonate, and evaporation of the dried ($Na_2SO_4$) solution, gave a solid residue (1 g.). Recrystallisation from ether–light petroleum (b. p. 60—80°) gave needles of the trans-*monoacetate*, m. p. 92° (Found: C, 69·9; H, 7·1. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%).

Treatment of the *trans*-monoacetate with toluene-*p*-sulphonyl chloride (1·1 mol.) in pyridine at room temperature overnight, followed by dilution with cold water, gave an oil which slowly solidified. Recrystallisation from methanol gave the trans-*acetate toluene*-p-*sulphonate*, needles, m. p. 85° (Found: C, 62·9; H, 5·7; S, 8·9. $C_{19}H_{20}O_5S$ requires C, 63·3; H, 5·6; S, 8·9%).

*Monotoluene*-p-*sulphonate of Tetralin*-trans-2 : 3-*diol*.—A solution of 2 : 3-epoxytetralin (7·0 g.) in dry ether (20 c.c.) was added dropwise to a stirred suspension of toluene-*p*-sulphonic acid (13 g.) in dry ether (30 c.c.) at room temperature; the reaction mixture became warm. It was set aside for 24 hr., then washed with water until neutral, dried ($Na_2SO_4$), and evaporated to a solid (12·3 g., 80%) which, on recrystallisation from ether–light petroleum (b. p. 60—80°), gave the trans-*monotoluene*-p-*sulphonate*, plates, m. p. 88—89° (Found: C, 63·8; H, 5·8; S, 9·9. $C_{17}H_{18}O_4S$ requires C, 64·1; H, 5·7; S, 10·1%).

Treatment of the *trans*-monotoluene-*p*-sulphonate with slight excess of the appropriate acid chloride in pyridine at room temperature overnight, followed by dilution with water, gave the *trans*-ditoluene-*p*-sulphonate, plates (from methanol), m. p. and mixed m. p. 143—144°; the trans-*methanesulphonate toluene*-p-*sulphonate*, needles (from methanol), m. p. 133—134° (Found: C, 54·5; H, 5·2; S, 16·05. $C_{18}H_{20}O_6S_3$ requires C, 54·5; H, 5·1; S, 16·2%); and the trans-*benzoate toluene*-p-*sulphonate*, felted needles (from methanol), m. p. 160° (Found: S, 7·5. $C_{24}H_{22}O_5S$ requires S, 7·6%).

The monotoluene-*p*-sulphonate with acetic anhydride in pyridine gave the *trans*-acetate toluene-*p*-sulphonate, m. p. and mixed m. p. 85°.

*Monomethanesulphonate of Tetralin*-trans-2 : 3-*diol*.—2 : 3-Epoxytetralin (2·8 g.) in dry

[22] Prajer, *Roczniki Chem.*, 1954, **28**, 55.
[23] Sand and Genssler, *Ber.*, 1903, **36**, 3705.
[24] Verkade, Coops, Maan, and Verkade-Sandbergen, *Annalen*, 1928, **467**, 217.

ether (10 c.c.) was treated with methanesulphonic acid (2·3 g.) in dry ether (20 c.c.) as for the reaction with toluene-*p*-sulphonic acid. A crystalline solid soon began to separate and next day it was collected and washed twice with a little ether (yield, 4 g., 86%; m. p. 100°). Recrystallisation from 1 : 1 aqueous methanol gave the trans-*monomethanesulphonate*, needles, m. p. 103° (Found: C, 54·6; H, 6·0; S, 13·0. $C_{11}H_{14}O_4S$ requires C, 54·5; H, 5·8; S, 13·2%).

Reaction of the product with methanesulphonyl chloride (1·3 mol.) in pyridine at room temperature gave the *trans*-dimethanesulphonate, m. p. and mixed m. p. 141°.

The monomethanesulphonate (2·1 g.) with acetic anhydride (2 g.) in pyridine (4 c.c.) gave the trans-*acetate methanesulphonate* (2·25 g.), prisms (from methanol), m. p. 95° (Found: S, 11·2. $C_{13}H_{16}O_5S$ requires S, 11·3%).

*Monoacetate of Tetralin*-cis-2 : 3-*diol*.—(i) A mixture of the *trans*-acetate toluene-*p*-sulphonate (7·5 g.), calcium carbonate (8 g.), acetone (50 c.c.), and water (50 c.c.) was heated on the steam-bath for 48 hr. The mixture was then cooled and filtered, and the acetone removed under reduced pressure, whereupon an oil separated from the aqueous residue. When cooled, the oil solidified (3·1 g., 72%; m. p. 95—97°), and on recrystallisation from aqueous methanol gave the cis-*monoacetate*, needles, m. p. 98° (Found: C, 69·9; H, 6·9. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%).

(ii) The *trans*-acetate methanesulphonate (2·45 g.) on similar treatment with calcium carbonate (2·9 g.) in 50% aqueous acetone (50 c.c.) gave the *cis*-monoacetate (1·1 g., 62%), m. p. and mixed m. p. 98°.

A solution of the *cis*-monoacetate (0·6 g.) in methanol (10 c.c.) containing sodium methoxide (from 0·05 g. of sodium) was boiled under reflux for 30 min. Neutralisation with carbon dioxide, followed by evaporation to dryness and treatment with a little water, afforded a crystalline residue which was recrystallised from water, to give the *cis*-diol (0·4 g.), m. p. and mixed m. p. 124°.

Treatment of the *cis*-monoacetate with toluene-*p*-sulphonyl chloride in pyridine gave the cis-*acetate toluene*-p-*sulphonate*, prisms (from methanol), m. p. 128° (Found: C, 63·4; H, 5·6; S, 8·8. $C_{19}H_{20}O_5S$ requires C, 63·3; H, 5·6; S, 8·9%).

*Monotoluene*-p-*sulphonate of Tetralin*-cis-2 : 3-*diol*.—A solution of toluene-*p*-sulphonyl chloride (5·23 g., 1 mol.) in dry pyridine (50 c.c.), cooled to 0°, was added in small portions to a solution of tetralin-*cis*-2 : 3-diol (4·5 g.) in pyridine (40 c.c.) also at 0° during 3 days. The solution was kept at 0° for another 2 days, then diluted with ice and water; the insoluble brown oil solidified on prolonged trituration. Recrystallisation from ether–light petroleum (b. p. 60—80°) gave the cis-*monotoluene*-p-*sulphonate* (3·2 g., 37%), m. p. 107° (Found: C, 64·1; H, 5·9; S, 9·95. $C_{17}H_{18}O_4S$ requires C, 64·1; H, 5·7; S, 10·1%).

Treatment of the *cis*-monotoluene-*p*-sulphonate with acetic anhydride in pyridine gave the *cis*-acetate toluene-*p*-sulphonate, m. p. and mixed m. p. 128°.

2 : 3-*Epoxytetralin from the Monotoluene*-p-*sulphonate and the Monomethanesulphonate of Tetralin*-trans-2 : 3-*diol*.—(i) The *trans*-monotoluene-*p*-sulphonate (0·5 g.) was dissolved in a mixture of 5% aqueous sodium hydroxide (20 c.c.) and methanol (25 c.c.), and kept at room temperature for 30 min. Dilution with water and extraction with ether gave the epoxide, which after recrystallisation from light petroleum (b. p. 60—80°) had m. p. and mixed m. p. 42°.

(ii) The *trans*-monomethanesulphonate, on similar treatment gave the epoxide, m. p. and mixed m. p. 42°.

β-*Tetralone from the Monotoluene*-p-*sulphonate of Tetralin*-cis-2 : 3-*diol*.—The *cis*-monotoluene-*p*-sulphonate (0·4 g.) was suspended in 0·5N-sodium hydroxide (10 c.c.) and steam-distilled until the distillate became clear. A portion of the distillate, treated with a drop of alkali and shaken for a few seconds, gave the deep blue colour characteristic of β-tetralone; another portion gave the semicarbazone, m. p. and mixed m. p. 190° (from ethanol).

*Reactions of the Monotoluene*-p-*sulphonates of Tetralin*-2 : 3-*diol with Lithium Chloride*.—(i) A mixture of the *trans*-monotoluene-*p*-sulphonate (1·2 g.), lithium chloride (1 g.), and ethanol (10 c.c.) was refluxed on the steam-bath for 24 hr. Removal of the solvent followed by dilution with water precipitated *trans*-3-chlorotetralin-2-ol, which after recrystallisation from aqueous methanol formed needles (0·48 g., 70%), m. p. 117° (lit.,[4] m. p. 117·5°).

(ii) Similar treatment of the *cis*-monotoluene-*p*-sulphonate (0·4 g.) with lithium chloride (0·4 g.) in ethanol (10 c.c.) gave a liquid product which formed a precipitate on treatment with 2 : 4-dinitrophenylhydrazine sulphate, but no pure derivative could be isolated.

4 : 5-*Epoxy*cyclo*hexene*.—*cyclo*Hexa-1 : 4-diene, prepared by dehydration of quinitol with

XUM

sulphuric acid,[25] and carefully fractionated through a 50 × 2 cm. Fenske column, had b. p. 88·5—89·5°/764 mm., $n_D^{24}$ 1·4700 (lit.,[26] b. p. 88·7—88·9°/764 mm., $n_D^{20}$ 1·4725). The light absorption in EtOH, $\lambda_{max.}$ 2560 Å (ε 52), indicated the presence of less than 1% of the 1 : 3-diene.

Solutions of the 1 : 4-diene (24·7 g.) in chloroform (100 c.c.), and of perbenzoic acid (48·1 g). in chloroform (590 c.c.) were separately cooled to −10°, and the latter was then added to the former at the same temperature in portions of 10 c.c. during 7 days. The mixture was kept for two more days in the refrigerator and was then washed with ice-cold 10% aqueous sodium hydroxide and with water, and dried ($Na_2SO_4$). Most of the solvent was then removed on the steam-bath through a column, and the residue was distilled through a short Vigreux column, to give 4 : 5-epoxy*cyclo*hexene (17·5 g., 59%), b. p. 39—40°/11 mm., $n_D^{20}$ 1·4810 (Found: C, 75·0; H, 8·6. Calc. for $C_6H_8O$: C, 75·0; H, 8·4%) (lit.,[27] b. p. 41—43°/14 mm.).

cyclo*Hex*-4-*ene*-trans-1 : 2-*diol*.—A mixture of 4 : 5-epoxy*cyclo*hexene (9·6 g.), acetic acid (6 g.), and water (90 c.c.) was heated on the steam-bath for 4 hr.; it was then cooled, neutralised with solid sodium hydrogen carbonate, saturated with sodium chloride, and extracted with ether (3 × 50 c.c.). The dried ($Na_2SO_4$) extracts were evaporated to a solid (5·8 g.), m. p. 94—96°. The aqueous solution on continuous extraction with ether gave more solid (4·6 g.), m. p. 96—97°. The combined product was recrystallised from light petroleum (b. p. 80—100°), to give *cyclo*hex-4-ene-*trans*-1 : 2-diol (9·3 g., 82%), prisms, m. p. 97° (lit.,[15] m. p. 96°) (Found: C, 63·2; H, 9·1. Calc. for $C_6H_{10}O_2$: C, 63·1; H, 8·8%). Infrared absorption: see Table.

Treatment of the diol with toluene-*p*-sulphonyl chloride (2·1 mol.) in pyridine at room temperature for 12 hr. gave the trans-*ditoluene*-p-*sulphonate*, prisms (from methanol), m. p. 116° (Found: C, 56·7; H, 5·5; S, 15·4. $C_{20}H_{22}O_6S_2$ requires C, 56·85; H, 5·25; S, 15·2%).

*Monotoluene*-p-*sulphonate of* cyclo*Hex*-4-*ene*-trans-1 : 2-*diol*.—A solution of 4 : 5-epoxy-*cyclo*hexene (15·7 g.) in dry ether (100 c.c.) was slowly added to a stirred suspension of toluene-*p*-sulphonic acid (42 g.) in dry ether (80 c.c.) at 0°. The stirring was continued for 1 hr. at room temperature and the solution was then washed with water until neutral, dried ($Na_2SO_4$), and evaporated to a solid residue (39 g.), m. p. 65—66°. Recrystallisation from ether–light petroleum (b. p. 40—60°) gave the *trans*-monotoluene-*p*-sulphonate, needles, m. p. 67° (Found: C, 58·2; H, 6·25; S, 11·7. $C_{13}H_{16}O_4S$ requires C, 58·2; H, 6·0; S, 11·95%). On reaction with toluene-*p*-sulphonyl chloride in pyridine this gave the *trans*-ditoluene-*p*-sulphonate, m. p. and mixed m. p. 116°.

Treatment of the *trans*-monotoluene-*p*-sulphonate (39 g.) in pyridine (80 c.c.) with acetic anhydride (20 g.) for 36 hr. at 0°, followed by dilution with water, and recrystallisation of the precipitated solid from aqueous methanol gave the trans-*acetate toluene*-p-*sulphonate* (43 g.), needles, m. p. 87—88° (Found: C, 58·3; H, 6·1. $C_{15}H_{18}O_6S$ requires C, 58·0; H, 5·8%).

*Monoacetate of* cyclo*Hex*-4-*ene*-cis-1 : 2-*diol*.—A mixture of the *trans*-acetate toluene-*p*-sulphonate (20 g.), calcium carbonate (20 g.), acetone (165 c.c.), and water (165 c.c.) was boiled on the steam-bath for 48 hr. After filtration, the solution was concentrated under reduced pressure, then saturated with sodium chloride and extracted continuously with ether, to give an oil, which on distillation furnished the cis-*monoacetate* (9·35 g., 93%), b. p. 94°/2 mm., $n_D^{23}$ 1·4792 (Found: C, 62·1; H, 8·2. $C_8H_{12}O_3$ requires C, 61·5; H, 7·8%).

Treatment of the product with toluene-*p*-sulphonyl chloride in pyridine gave the cis-*acetate toluene*-p-*sulphonate*, prisms (from methanol), m. p. 85° (Found: C, 57·7; H, 5·6; S, 10·4. $C_{15}H_{18}O_6S$ requires C, 58·0; H, 5·8; S, 10·3%). A mixed m. p. with the *trans*-isomer was 60—63°.

cyclo*Hex*-4-*ene*-cis-1 : 2-*diol*.—A solution of the *cis*-monoacetate (9 g.) and sodium (0·08 g.) in methanol (80 c.c.) was refluxed for 30 min., then cooled, neutralised with carbon dioxide, and concentrated under reduced pressure. The residue was dissolved in water (5 c.c.), saturated with sodium chloride, and extracted with ether to give the *cis*-diol (6·3 g., 96%), which crystallised from ether–light petroleum (b. p. 60—80°) in flakes, m. p. 80—81° (lit.,[14] m. p. 80·3—81·1°) (Found: C, 63·2; H, 9·0. Calc. for $C_6H_{10}O_2$: C, 63·1; H, 8·8%). Infrared absorption: see Table.

Treatment of the *cis*-diol with toluene-*p*-sulphonyl chloride (2 mol.) in pyridine for 12 hr. at room temperature gave the cis-*ditoluene*-p-*sulphonate*, prisms (from methanol), m. p. 110° (Found: C, 56·9; H, 5·6; S, 15·2. $C_{20}H_{22}O_6S_2$ requires C, 56·85; H, 5·25; S, 15·2%).

[25] Senderens, *Compt. rend.*, 1923, **177**, 1183.
[26] Wibaut and Haak, *Rec. Trav. chim.*, 1948, **67**, 85.
[27] Tiffeneau and Tchoubar, *Compt. rend.*, 1941, **212**, 581.

*Monotoluene*-p-*sulphonate of* cyclo*Hex*-4-*ene*-cis-1 : 2-*diol*.—A solution of toluene-*p*-sulphonyl chloride (5 g.) in pure dry chloroform (35 c.c.) was added to a solution of the *cis*-diol (3 g.) in pyridine (8 c.c.) in small portions during 3 days at 0°. The mixture was kept at 0° for a further 24 hr. and it was then diluted with chloroform, washed with dilute sulphuric acid, aqueous sodium hydrogen carbonate, and water and dried ($Na_2SO_4$). Removal of the solvent gave an oil which was dissolved in boiling ether (20 c.c.); light petroleum (b. p. 40—60°) was added to faint turbidity and the mixture was left in the refrigerator. A solid (4·3 g.), m. p. 70—72°, separated and on fractional crystallisation from methanol gave the *cis*-ditoluene-*p*-sulphonate (0·8 g., 7%), m. p. and mixed m. p. 110°, and the cis-*monotoluene*-p-*sulphonate* (2·3 g., 33%), needles, m. p. 78° (Found: C, 58·3; H, 6·3; S, 11·5. $C_{13}H_{16}O_4S$ requires C, 58·2; H, 6·0; S, 11·95%).

Treatment of the *cis*-monotoluene-*p*-sulphonate in pyridine with a slight excess of toluene-*p*-sulphonyl chloride gave the *cis*-ditoluene-*p*-sulphonate, m. p. and mixed m. p. 110°.

*Reactions of the Monotoluene*-p-*sulphonates of* cyclo*Hex*-4-*ene*-1 : 2-*diol with Alkali*.—(i) The *trans*-monotoluene-*p*-sulphonate when shaken with 10% aqueous sodium hydroxide at room temperature gave 4 : 5-epoxy*cyclo*hexene (characteristic odour). The acidified mixture gave no precipitate with 2 : 4-dinitrophenylhydrazine sulphate. Similar treatment of the *cis*-isomer gave a solution which gave a positive reaction with the latter reagent.

(ii) The *cis*-monotoluene-*p*-sulphonate (0·5 g.), suspended in 10% aqueous sodium hydroxide (10 c.c.), was steam-distilled. Treatment of the distillate with aqueous 2 : 4-dinitrophenylhydrazine sulphate gave *cyclo*hex-2-enone 2 : 4-dinitrophenylhydrazone, orange needles (from methanol), m. p. 162—163° (Found: C, 51·95; H, 4·55; N, 19·9. Calc. for $C_{12}H_{12}O_4N_4$: C, 52·2; H, 4·4; N, 20·3%), $\lambda_{max.}$ (in $CHCl_3$) 3770 Å (ε 27,000). Birch [25] gives m. p. 165—166°. The derivative of *cyclo*hex-3-enone [25] has m, p. 131—132°.

*Quantitative Alkaline Hydrolysis of the Monotoluene*-p-*sulphonates*.—(i) Tetralin-*trans*-2 : 3-diol monotoluene-*p*-sulphonate (1·1555 g.) was dissolved in methanol (80 c.c.) and kept at 19°. A 5-c.c. portion was diluted with 40 c.c. of methanol at 19° and then rapidly mixed with 5 c.c. of 0·0837N-methanolic potassium hydroxide at 19°, thus giving a 0·00454M-solution of the ester in 0·00837N-alkali, and kept at this temperature for a known time. 0·1N-Hydrochloric acid (10 c.c.) was then rapidly added, and the excess of acid was titrated with standard alkali, bromophenol-blue being used as indicator.

The % reaction was: 64 (1 min.); 83 (2 min.); 89 (3 min.). The corresponding values of $k_2$ were 157, 155, and 133 mole$^{-1}$ l. min.$^{-1}$.

(ii) Tetralin-*cis*-2 : 3-diol monotoluene-*p*-sulphonate (0·8508 g.) was dissolved in 0·0837N-methanolic potassium hydroxide (80 c.c.) at 19° (to give a 0·0334M-solution of the ester) and kept at that temperature under nitrogen. A 5 c.c.-portion was removed at intervals, added to 0·1N-hydrochloric acid (10 c.c.), and back-titrated with alkali. The % reaction was: 24 (1·5 hr.), 43 (3·5 hr.), 54 (5 hr.), 67 (7 hr.), 76 (9 hr.); and the corresponding values of $k_2$ were 0·038, 0·035, 0·035, 0·038, 0·039 mole$^{-1}$ l. min.$^{-1}$.

(iii) For *cyclo*hex-4-ene-*trans*-1 : 2-diol monotoluene-*p*-sulphonate the method described in (i) was used, the rate measurements being made on a 0·00354M-solution of the ester in 0·00819N-methanolic potassium hydroxide. The % reaction was: 59 (1 min.), 74 (2 min.), 85 (3 min.), 90 (4 min.); and the corresponding values of $k_2$ were 130, 103, 104, and 98 mole$^{-1}$ l. min.$^{-1}$.

(iv) *cyclo*Hex-4-ene-*cis*-1 : 2-diol monotoluene-*p*-sulphonate, as a 0·0351M-solution in 0·0819N-methanolic potassium hydroxide, gave the following values for % reaction: 19 (2 hr.), 32 (3·5 hr.), 39 (5 hr.), 54 (8 hr.); and respective $k_2$ values of 0·023, 0·024, 0·023, 0·023 mole$^{-1}$ l. min.$^{-1}$.

*Rates of Oxidation of the Tetralin*-2 : 3-*diols with Lead Tetra-acetate*.—Rates for the *cis*- and for the *trans*-diol, in acetic acid at 25°, were determined by Cordner and Pausacker's method,[19] bimolecular rate constants being calculated from the slopes of the plots of $\log_{10} b(a - x)/a(b - x)$ against $t$. Results are given in the Table. As a control, a run was carried out on *cyclo*hexane-*trans*-1 : 2-diol, which gave $k_2$ = 0·33 mole$^{-1}$ l. min.$^{-1}$. Eliel and Pillar [17] give 0·316.

This work, and that described in the following paper, was carried out during the tenure (by M. E. A.) of a Foreign Scholarship awarded by the Government of Pakistan.

Department of Organic Chemistry, Imperial College of Science and Technology, South Kensington, London, S.W.7. [*Received, November 7th*, 1957.]

[19] Birch, *J.*, 1946, 593.
[19] Cordner and Pausacker, *J.*, 1953, 102.

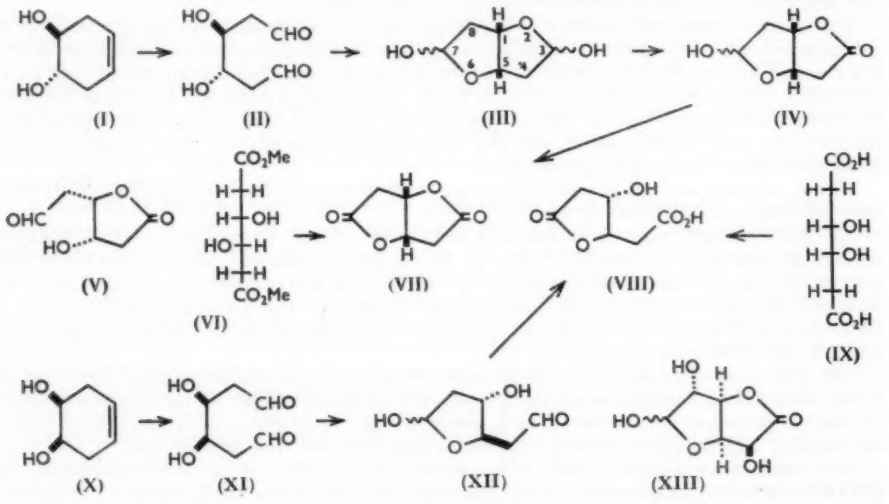
XUM

## 213. *Alicyclic Glycols. Part XV.*[1] *Some Lactols and Lactones Derived from the* cyclo*Hex*-4-*ene*-1 : 2-*diols.*

By Md. Erfan Ali and L. N. Owen.

Ozonolysis of *cyclo*hex-4-ene-*trans*- and -*cis*-1 : 2-diol, followed by further oxidation, yields respectively the $\gamma\gamma$-dilactone of (±)-ββ′-dihydroxyadipic acid and the γ-lactone of the *meso*-acid. (±)-ββ′-Dihydroxyadipdialdehyde exists as the crystalline bicyclic hemiacetal (III).

By treatment of *cis-cis*-muconic acid with aqueous hydrochloric or sulphuric acid, Linstead and his co-workers [2] obtained a compound which they suggested was probably the dilactone (VII) of (±)-ββ′-dihydroxyadipic acid, on the assumption that a *cis*-fused bicyclic system would be preferred. Although it has subsequently been shown [3] that the *trans*-fusion of two five-membered rings can occur with unexpected ease, the structure (VII) was suported by the observation [4, 5] that the same dilactone was obtained by hydrolysis of a dimethyl ββ′-dihydroxyadipate which, from its method of preparation (*cis*-hydroxylation of dimethyl *trans*-$\Delta^{\beta}$-dihydromuconic acid with permanganate [4] or with hydrogen peroxide–*tert.*-butyl alcohol–osmium tetroxide [5]), could be assigned the (±)-configuration (VI). This conclusion has recently been confirmed [6] by resolution of the corresponding (±)-acid, which is also readily converted into the same dilactone (VII).




When *trans*-$\Delta^{\beta}$-dihydromuconic acid was treated with performic acid it gave,[4] presumably *via meso*-ββ′-dihydroxyadipic acid (IX), the hydroxy-lactonic acid (VIII), which showed no tendency to give a *trans*-fused dilactone. The experiments described below, which were in progress when the resolution of the (±)-acid was reported, provide independent proof of these configurations by correlation with the *cyclo*hex-4-ene-1 : 2-diols.[1]

Ozonolysis of *cyclo*hex-4-ene-*trans*-1 : 2-diol (I) furnished a crystalline product, $C_6H_{10}O_4$, which gave a bis-*p*-nitrophenylhydrazone and a dioxime, but it reacted only very slowly

[1] Part XIV, Ali and Owen, preceding paper.
[2] Elvidge, Linstead, Orkin, Sims, Baer, and Pattison, *J.*, 1950, 2228; Elvidge, Linstead, Sims, and Orkin, *ibid.*, p. 2235.
[3] Owen and Peto, *J.*, 1955, 2383.
[4] Linstead, Owen, and Webb, *J.*, 1953, 1225.
[5] Legrand, *Bull. Soc. chim. France*, 1953, 540.
[6] Posternak and Susz, *Helv. Chim. Acta*, 1956, **39**, 2032.

with Schiff's reagent and was devoid of carbonyl absorption in the infrared spectrum. The (±)-dialdehyde (II) therefore exists entirely as the bicyclic double hemiacetal, (±)-*cis*-2 : 6-dioxa*bicyclo*[3 : 3 : 0]octane-3 : 7-diol (III), in which the *cis*-fusion of the two rings follows from the *trans*-disposition of the hydroxyl groups in the original diol. There are three possible stereoisomers of (III), according to the configurations of the hydroxyl groups (*endo-cis*, *exo-cis*, and *trans*), but a choice is not possible on the evidence available. Only one of the potential aldehydic groups in (III) was oxidised by aqueous bromine at room temperature, the product being a crystalline monolactone, (±)-7-hydroxy-*cis*-2 : 6-dioxa*bicyclo*[3 : 3 : 0]octan-3-one (IV); its infrared spectrum showed absorption at 1779 cm.$^{-1}$, due to the presence of the carbonyl group in the γ-lactone ring, but ordinary carbonyl absorption was again absent. The hemiacetal ring in this compound was markedly more stable than those in its precursor (III), for it was quite unreactive towards Schiff's reagent; it did, however, react with *p*-nitrophenylhydrazine to give the derivative of *cis*-tetrahydro-3-hydroxy-5-oxo-2-furylacetaldehyde (V). More vigorous treatment of the monolactone (IV), with aqueous bromine at 70°, gave the γγ-dilactone (VII) of (±)-ββ′-dihydroxyadipic acid, identical with that obtained earlier.

Ozonolysis of *cyclo*hex-4-ene-*cis*-1 : 2-diol gave a non-crystalline aldehydic product which was probably mainly the monohemiacetal (XII) of *meso*-ββ′-dihydroxyadipdialdehyde (XI), though no satisfactory crystalline carbonyl derivatives could be prepared. On oxidation with an excess of aqueous bromine, however, it readily gave the crystalline lactonic acid (VIII).

The infrared spectra of the three lactones (IV), (VII), and (VIII) in chloroform solution showed a single absorption maximum near 1780 cm.$^{-1}$, consistent [7] with the γ-lactone structure. In paraffin mull the lactones (VII) and (VIII) still showed absorption at 1780 ± 10 cm.$^{-1}$, though the bands were complex; the absorption maximum of (IV), however, moved to 1756 and 1742 cm.$^{-1}$ (doublet), presumably owing to intermolecular bonding between the hydroxy- and the carbonyl group. This lactone is a simple analogue of glucurone (XIII), and for comparison the infrared absorption of the latter, which undoubtedly is a γ-lactone, was also measured in paraffin mull; it showed a maximum at 1751 cm.$^{-1}$. Since the quoted [7] range for the carbonyl absorption band in δ-lactones is 1750—1735 cm.$^{-1}$, misleading conclusions could clearly be reached when measurements are made, other than in dilute solution, on γ-lactones containing other functions capable of bonding to the carbonyl group.

Barker and Stephens [8] have reported that compounds containing a furanose or hydrofuranol ring, including those with two fused five-membered rings, show characteristic infrared absorption in the 1000—700 cm.$^{-1}$ range, the maxima being usually located within four distinct regions. The frequencies of the absorption maxima shown in that range by our compounds (III), (IV), (VII), and (VIII), however, cannot all be accommodated within the limits quoted for these four regions.

## Experimental

Analyses were by Miss J. Cuckney and staff, and infrared spectra by Mr. R. L. Erskine, B.Sc., A.R.C.S. The absorption maxima refer to the regions 4000—1500 and 1000—700 cm.$^{-1}$ in paraffin mull, and 2000—1500 cm.$^{-1}$ in $CHCl_3$.

*Ozonolysis of* cyclo*Hex*-4-*ene*-trans-1 : 2-*diol*.—Ozonised oxygen was passed through a solution of the *trans*-diol (4·2 g.) in dry ethyl acetate (225 c.c.) at −20° until no more was absorbed. The solution was then hydrogenated over 2% palladium–calcium carbonate (0·5 g.), with cooling. After filtration, the solution was evaporated and the residue, m. p. 103—106°, was recrystallised from ethyl acetate to give (±)-*cis*-2 : 6-*dioxa*bicyclo[3 : 3 : 0]*octane*-3 : 7-*diol* (2·5 g., 47%), plates, m. p. 110° (Found: C, 49·2; H, 7·0. $C_8H_{12}O_4$ requires C, 49·3; H, 6·9%). It was very sparingly soluble in ether, light petroleum, and chloroform, but readily soluble

[7] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen and Co., London, 1954.
[8] Barker and Stephens, *J.*, 1954, 4550.

XUM

in water. With Schiff's reagent, a colour appeared after *ca.* 3 min. Infrared absorption in paraffin mull: $\nu_{max.}$ 3344 (O–H), 964, 907, 859, 825, 810 cm.$^{-1}$; no absorption in the 1600—1800 cm.$^{-1}$ region.

A mixture of the compound (0·07 g.), *p*-nitrophenylhydrazine (0·18 g.), and ethanol (3 c.c.), refluxed for 30 min. and then diluted with water, gave a precipitate which was washed with boiling methanol and then dissolved in boiling dioxan (15 c.c.). Dilution of the solution with light petroleum (b. p. 40—60°) gave (±)-3 : 4-*dihydroxyhexanedial bis*-p-*nitrophenylhydrazone* (0·19 g., 95%) as a yellow powder, m. p. 205° (Found: C, 52·0; H, 5·2; N, 19·6. $C_{18}H_{20}O_6N_6$ requires C, 51·9; H, 4·8; N, 20·2%).

Reaction of the *bicyclo*-compound (0·1 g.) with hydroxylamine hydrochloride (0·15 g.) and sodium acetate (0·25 g.) in water (2 c.c.) for 1 hr. at 40°, followed by 24 hr. at room temperature, gave a precipitate which on recrystallisation from methanol gave the slightly impure *dioxime*, m. p. 170° (decomp.), of (±)-3 : 4-dihydroxyhexanedial (Found: C, 41·9; H, 7·2; N, 15·1. $C_6H_{12}O_4N_2$ requires C, 40·9; H, 6·9; N, 15·9%).

(±)-7-*Hydroxy*-cis-2 : 6-*dioxa*bicyclo[3 : 3 : 0]*octan*-3-*one*. Bromine (2·2 g.) was added to a solution of the above dihydroxy*bicyclo*-compound (1 g.) in water (25 c.c.), and the mixture was shaken for 5 hr. and left overnight at room temperature. The remaining bromine was then removed in a current of nitrogen, and the colourless solution was neutralised with silver carbonate, filtered, then saturated with hydrogen sulphide and again filtered. The filtrate was continuously extracted with ether, to yield a solid (0·5 g.) which after three recrystallisations from ethyl acetate gave (±)-7-*hydroxy*-cis-2 : 6-*dioxa*bicyclo[3 : 3 : 0]*octan*-3-*one* (0·23 g., 22%), prisms, m. p. 100° (Found: C, 50·1; H, 5·65. $C_6H_8O_4$ requires C, 50·0; H, 5·6%). It gave no colour with Schiff's reagent even after several hours, and gave a neutral aqueous solution. Infrared absorption, in paraffin mull: $\nu_{max.}$ 3356 (O–H), 1756 and 1742 (C=O in lactone), 988, 923, 897, 864, 836, 824, 806, 778 cm.$^{-1}$; in $CHCl_3$: $\nu_{max.}$ 1779 cm.$^{-1}$.

Treatment of a portion (0·13 g.) with *p*-nitrophenylhydrazine (0·13 g.) in boiling ethanol (10 c.c.) for 30 min., followed by dilution with water and recrystallisation of the precipitate from methanol, gave *tetrahydro*-3-*hydroxy*-5-*oxo*-2-*furylacetaldehyde* p-*nitrophenylhydrazone* (0·24 g., 95%), yellow needles, m. p. 148° (Found: C, 51·45; H, 4·85; N, 15·0. $C_{12}H_{13}O_5N_3$ requires C, 51·6; H, 4·7; N, 15·05%).

(±)-2 : 6-*Dioxa*bicyclo[3 : 3 : 0]*octane*-3 : 7-*dione*.—A mixture of the above monolactone (0·2 g.), water (2 c.c.), and bromine (0·25 g.) was heated at 70° in a sealed tube for 7 hr. with occasional shaking. Next day, a trace of unchanged bromine was removed by a stream of nitrogen, and the solid (0·05 g.) which had separated from the solution in hard prisms, m. p. 132°, was collected. The m. p. was unchanged by recrystallisation of the compound from ethyl acetate, and the mixed m. p. with an authentic sample [4] of (±)-2 : 6-dioxa*bicyclo*[3 : 3 : 0]octane-3 : 7-dione, m. p. 130—131°, was undepressed. A further quantity (0·13 g.) was isolated by concentration of the aqueous mother-liquor (total yield, 66%). Infrared absorption, in paraffin mull: $\nu_{max.}$ 1789, 1774, and 1759 (C=O in γ-lactone), 929, 892, 841, 818 cm.$^{-1}$; in $CHCl_3$: $\nu_{max.}$ 1783 cm.$^{-1}$.

*Ozonolysis of* cyclo*Hex*-4-*ene*-cis-1 : 2-*diol* (with M. H. Benn).—A solution of the *cis*-diol (1·7 g.) in pure dry ethyl acetate (130 c.c.) was ozonised, and the solution subsequently hydrogenated, in the same way as described for the *trans*-isomer. Evaporation of the filtered solution gave a viscous acidic syrup (1·6 g.) which gave an immediate colour with Schiff's reagent and an amorphous precipitate with 2 : 4-dinitrophenylhydrazine sulphate; no crystalline carbonyl derivatives could be obtained.

trans-γ-*Carboxymethyl*-β-*hydroxybutanolide*.—A mixture of the above syrup (0·4 g.), bromine (1·2 g.), and water (10 c.c.) was kept at 45—50° for 3 hr. with occasional shaking. The excess of bromine was then removed in a stream of nitrogen, and sodium hydrogen carbonate was gradually added to the colourless solution to neutralise only the hydrogen bromide (*i.e.*, until only a dull blue colour was produced on Congo paper). The solution was evaporated to dryness under reduced pressure, and the residue was kept at 70°/15 mm. for 30 min. and then extracted with boiling ethyl acetate. Evaporation of the filtered extracts gave a pale yellow oil which partly crystallised. The solid (0·25 g.) was drained on porous tile and recrystallised from ethyl acetate, to give *trans*-γ-carboxymethyl-β-hydroxybutanolide, m. p. 98°. Infrared absorption, in paraffin mull: $\nu_{max.}$ 3472 (O–H), 2700—2600 (O–H in $CO_2H$, dimeric form), 1786 and 1770 (C=O in γ-lactone), 1709 (C=O in $CO_2H$), 980, 930, 908, 877, 832 cm.$^{-1}$; in $CHCl_3$: $\nu_{max.}$ 1777, 1715 cm.$^{-1}$.

XUM

The quoted [4] m. p. is 91°, but re-examination of the original specimen showed it to have m. p. 97°; a mixed m. p. with the acid now obtained was undepressed.

DEPARTMENT OF ORGANIC CHEMISTRY, IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, SOUTH KENSINGTON, LONDON, S.W.7. [*Received, November 7th*, 1957.]

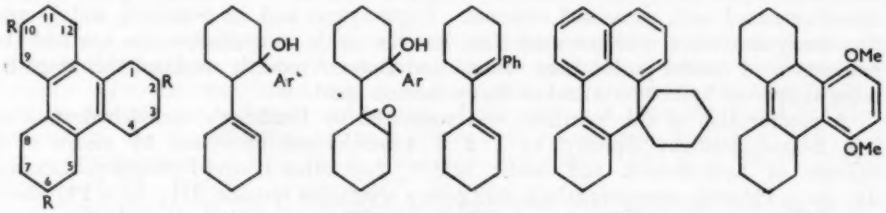
## 214. *Triphenylene: an Examination of Modified Mannich Syntheses, and an Improvement of the Rapson Synthesis.*

By C. C. BARKER, R. G. EMMERSON, and J. D. PERIAM.

The cyclodehydration of *cyclo*hexanone and its 2-, 3-, and 4-methyl derivative to dodecahydrotriphenylene (I; R = H) and its methyl derivatives, respectively, has been examined.

Rapson's triphenylene synthesis is improved by converting the 1-aryl-2-*cyclo*hexenyl*cyclo*hexanols (II) into the epoxy-derivatives (III) and cyclodehydrating these with hydrobromic–acetic acid. Triphenylene, 1- and 2-methyltriphenylene, and 1 : 2-benzochrysene are thus prepared.

THE simplest method of obtaining small quantities of triphenylene is by dehydrogenation of dodecahydrotriphenylene (I; R = H) prepared by cyclodehydration of *cyclo*hexanone with methanolic sulphuric acid.[1] Although the dodecahydrotriphenylene is obtained in a yield of only 6·5%, its isolation is simple and its dehydrogenation with palladised




(I) (II) (III) (IV) (V) (VI)

charcoal is almost quantitative. Attempts to improve this yield by means of alternative condensing agents have included the use of zinc chloride (3% yield),[2] thorium oxide at 300° (6·4% yield),[3] polyphosphoric acid (2% yield),[4] aluminium oxide at 320° (23% yield),[5] and a mixture of calcium and aluminium oxides with cerium oxide or thorium oxide at 290° (32% yield).[6] The last two processes are attractive and were investigated by us, but our best yield of dodecahydrotriphenylene amounted to only 13% and was obtained by heating purified *cyclo*hexanone with 13% of its weight of aluminium oxide containing 4·5% of thorium oxide at 280°/57 atm. for 32 hours. The presence of calcium oxide in this catalyst depressed the yield and quality of the product.

Similarly, cyclodehydration of 4-methyl*cyclo*hexanone by mixed aluminium and thorium oxides at 285°, or by boiling methanolic sulphuric acid, gave dodecahydro-2 : 6 : 10-trimethyltriphenylene (I; R = Me), which was easily dehydrogenated to 2 : 6 : 10-trimethyltriphenylene. The structure of the latter hydrocarbon follows from its method of preparation, and is supported by a comparison of its electronic absorption spectrum with the spectra of triphenylene [7] and its 1- and 2-methyl derivative (see Table). 2-Methyltriphenylene shows a bathochromic shift of 20 Å without change in intensity, whereas the

[1] Mannich, *Ber.*, 1907, **40**, 153.
[2] Kunze, *Ber.*, 1926, **59**, 2085.
[3] Komatsu and Masumoto, *Mem. Coll. Sci., Kyoto Univ.*, 1925, **19**, *A*, 15.
[4] Bavin and Dewar, *J.*, 1955, 4479.
[5] Petrov, *Bull. Soc. chim. France*, 1928, **43**, 1272; *J. Russ. Phys. Chem. Soc.*, 1928, **60**, 1435.
[6] B.P. 440,285/1935.
[7] Clar and Lombardi, *Ber.*, 1932, **65**, 1414.

1-isomer shows a bathochromic shift of 40 Å and a reduction in intensity. By analogy with similar compounds,[8] the spectroscopic effect of the 1-methyl group indicates that it is forced out of the plane of the remainder of the molecule. 2 : 6 : 10-Trimethyltriphenylene shows a bathochromic shift of 55 Å.

Attempted cyclodehydration of 2-methyl*cyclo*hexanone in the presence of oxides of aluminium and thorium at 285° gave none of the expected dodecahydro-1 : 5 : 9-trimethyltriphenylene, but large amounts of unchanged ketone were recovered and it is

*Ultraviolet absorption maxima* ($m\mu$) *in* EtOH ($10^{-5}\varepsilon$ in parentheses).

| Triphenylene derivative | λ | | λ | | λ | | λ | |
|---|---|---|---|---|---|---|---|---|
| Unsubst. | 284 | (0·17) | 273 | (0·19) | 257 | (1·51) | 248·5 | (0·87) |
| 1-Methyl | 288 | (0·14) | 279 | (0·16) | 261 | (1·05) | 253·5 | (0·74) |
| 2-Methyl | 285·5 | (0·16) | 275 | (0·18) | 259 | (1·51) | 250·5 | (0·84) |
| 2 : 6 : 10-Trimethyl | 288·5 | (0·17) | 277·5 | (0·20) | 262·5 | (1·50) | 253·5 | (0·87) |

likely that steric hindrance by the methyl group prevented reaction. This suggested that 3-methyl*cyclo*hexanone should give 2 : 6 : 10-trimethyltriphenylene, rather than the 1 : 7 : 11-, 1 : 7 : 9-, or 1 : 5 : 9-trimethyl isomer, but no crystalline substance was isolated after refluxing of the ketone with methanolic sulphuric acid.

The self-condensation of *cyclo*hexanone is also used in the first stage of Rapson's triphenylene synthesis,[9] in which 2-*cyclo*hex-1′-enyl*cyclo*hexanone is treated with an arylmagnesium halide to give an alcohol (II) which undergoes oxidative[4] cyclisation with aluminium chloride. The resultant 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydrotriphenylene is dehydrogenated with palladised charcoal. Triphenylene and its 2-methyl, and 1- and 2-methoxy-derivative were prepared thus, but the yields on cyclisation are low and the products need careful purification. Bavin and Dewar[4] recently modified this stage by using anhydrous hydrofluoric acid as the cyclisation agent.

A modification of this synthesis was suggested by Bradsher's cyclodehydration of 2-(1 : 2-epoxy*cyclo*hexyl)diphenyl to 1 : 2 : 3 : 4-tetrahydrotriphenylene by means of a mixture of hydrobromic and acetic acid.[10] 2-*cyclo*Hex-1′-enyl-1-phenyl*cyclo*hexanol (II; Ar = Ph) with monoperphthalic acid gave a crystalline epoxide (III; Ar = Ph) which was readily cyclodehydrated to 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydrotriphenylene in 50% overall yield; dehydrogenation of the crude cyclisation product gave triphenylene in 50% yield (based on the *cyclo*hexanol derivative). Attempts to use 2-*cyclo*hex-1′-enyl-1-phenyl-*cyclo*hexene (IV), formed as a by-product in the preparation of the corresponding alcohol, gave only 17% of triphenylene.

The preparation of 2-hydroxytriphenylene from 2-*cyclo*hex-1′-enyl-1-*p*-methoxyphenyl-*cyclo*hexanol (II; Ar = *p*-methoxyphenyl) has been described previously by us,[11] and 2-methyltriphenylene was readily obtained from the analogous alcohol (II; Ar = *p*-tolyl). Similarly, 1 : 2-benzochrysene was obtained from 2-*cyclo*hex-1′-enyl-1-α-naphthyl*cyclo*-hexanol (II; R = α-naphthyl); cyclisation of this alcohol with aluminium chloride, or anhydrous hydrofluoric acid, is known[4] to give only the spiran (V).

The method was less successful when applied to the preparation of 1-substituted triphenylenes. Thus 1-methyltriphenylene was obtained from the appropriate *cyclo*-hexanol (II; Ar = *o*-tolyl), but with greater difficulty; and although attempts to prepare 1 : 4-dimethyltriphenylene by cyclisation of 2-*cyclo*hex-1′-enyl-1-*p*-xylyl*cyclo*hexanol gave small amounts of crystalline material whose analysis was correct for 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydro-9 : 12-dimethyltriphenylene, dehydrogenation of the crude cyclisation product gave a hydrocarbon, m. p. 176·5—177°; Fieser and Joshel[12] give m. p. 108·4—109·2° for 1 : 4-dimethyltriphenylene. Further, 1-hydroxytriphenylene could not be obtained from

[8] Peters, *J.*, 1957, 646.
[9] Rapson, *J.*, 1941, 15.
[10] Bradsher, *J. Amer. Chem. Soc.*, 1939, **61**, 3131.
[11] Barker, Emmerson, and Periam, *J.*, 1955, 4482.
[12] Fieser and Joshel, *J. Amer. Chem. Soc.*, 1939, **61**, 2960.

2-*cyclo*hex-1′-enyl-*o*-methoxyphenyl*cyclo*hexanol (II; Ar = *o*-methoxyphenyl); instead, a small amount of triphenylene was obtained as end-product. This loss of a hydroxy(or methoxy)-group in the 1-position from a fully aromatic ring is consistent with our failure to isolate any product other than triphenylene after dehydrogenation of the decahydrodimethoxytriphenylene (VI), but it is not consistent with the smooth dehydrogenation of 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydro-9-methoxytriphenylene reported by Rapson.[9] Repetition of Rapson's work gave a mixture of triphenylene and 1-methoxytriphenylene which could be separated only by chromatography on alumina.

The use of *meta*-substituted Grignard reagents yields substituted *cyclo*hexanols which can cyclise in two ways. Thus, *cyclo*hex-1′-enyl-1-*m*-tolyl*cyclo*hexanol (II; Ar = *m*-tolyl) can give rise to 1- and 2-methyltriphenylene, but only the latter was isolated, although it is possible that some of the 1-isomer was formed. From *cyclo*hex-1′-enyl-1-β-naphthyl-*cyclo*hexanol (II; Ar = β-naphthyl), however, small amounts of 1 : 2 : 3 : 4-dibenzanthracene were isolated, together with a major yield of 1 : 2-benzochrysene.

## Experimental

*Cyclisation of* 2-cyclo*Hex*-1′-*enyl*-1-*phenyl*cyclo*hexanol*.—Monoperphthalic acid (4·3 g.) in ether (60 c.c.) was added to 2-*cyclo*hex-1′-enyl-1-phenyl*cyclo*hexanol (5·0 g.) in ether (50 c.c.) at 0°. The mixture was kept at 0° for 16 hr., then shaken with aqueous sodium hydrogen carbonate, dried ($Na_2SO_4$), and evaporated, giving 2-(1 : 2-*epoxy*cyclo*hexyl*)-1-*phenyl*cyclo*hexanol* (5·2 g.), m. p. 140° [from light petroleum (b. p. 60—80°)] (Found: C, 79·6; H, 8·6. $C_{18}H_{24}O_2$ requires C, 79·5; H, 8·8%).

The unpurified epoxide (5·1 g.) was refluxed with acetic acid (51 c.c.) and hydrobromic acid (34% w/w; 36 c.c.) for 12 hr. The brown solid which separated on cooling was dissolved in benzene, the solution was washed with aqueous sodium hydrogen carbonate and dried ($Na_2SO_4$), and the benzene was removed. Sublimation of the residue at 160—180° (bath)/$10^{-2}$ mm., followed by two crystallisations of the sublimate from ethanol gave 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydrotriphenylene (1·9 g.), m. p. 123° (Bavin and Dewar [4] give m. p. 125·5°) (Found: C, 91·6; H, 8·4. Calc. for $C_{18}H_{20}$: C, 91·5; H, 8·5%).

Dehydrogenation of the unpurified hydrocarbon with 30% palladised charcoal at 300° for 3 hr. and purification of the product by sublimation and crystallisation from benzene gave triphenylene, m. p. 198° (50%, based on the *cyclo*hexanol derivative).

2-*Methyltriphenylene*.—(*a*) *p*-Tolylmagnesium bromide with 2-*cyclo*hex-1′-enyl*cyclo*hexanone in ether gave 2-cyclo*hex*-1′-*enyl*-1-p-*tolyl*cyclo*hexanol* (50%), b. p. 135—136°/$10^{-2}$ mm. (Found: C, 84·5; H, 9·7. $C_{19}H_{26}O$ requires C, 84·5; H, 9·6%). This alcohol was converted into 2-methyltriphenylene, m. p. 103° (from ethanol), in 32% yield without purification of the intermediate epoxide or its cyclisation product; Fieser and Joshel [13] gave m. p. 102·6—103·6°.

(*b*) Formed in an analogous manner, 2-cyclo*hex*-1′-*enyl*-1-m-*tolyl*cyclo*hexano* (53% yield) boiled at 130—135°/$10^{-2}$ mm. (Found: C, 84·7; H, 9·9. $C_{19}H_{26}O$ requires C, 84·5; H, 9·6%) and gave the *epoxide* (90%), m. p. 104·5—106° (from ether) (Found: C, 80·1; H, 9·1. $C_{19}H_{26}O_2$ requires C, 79·7; H, 9·1%), which was cyclised to a yellow solid. This was dehydrogenated without purification. The product was sublimed ($10^{-2}$ mm.) and twice crystallised from ethanol, giving 2-methyltriphenylene (35%), m. p. 102—103°.

1-*Methyltriphenylene*.—*o*-Tolylmagnesium bromide and 2-*cyclo*hex-1′-enyl*cyclo*hexanone in ether gave 2-cyclo*hex*-1′-*enyl*-1-o-*tolyl*cyclo*hexanol* (28%), b. p. 132—134°/$10^{-2}$ mm. (Found: C, 83·6; H, 9·7%), whose *epoxide*, m. p. 172° (from ether) (Found: C, 80·2; H, 8·9%), was cyclised, the resultant hydrocarbon being distilled ($10^{-2}$ mm.) and fractionally eluted from alumina with 3 : 7 benzene–light petroleum (b. p. 60—80°), to give 1-methyltriphenylene (15%), m. p. 93—94° (from ethanol) (Fieser and Joshel [13] give m. p. 93·4—94·2°) (Found: C, 93·4; H, 5·8. Calc. for $C_{19}H_{14}$: C, 94·2; H, 5·8%).

*Cyclisation of* 2-cyclo*Hex*-1′-*enyl*-1-p-*xylyl*cyclo*hexanol*.—*p*-Xylylmagnesium bromide and 2-*cyclo*hex-1′-enyl*cyclo*hexanone gave 2-*cyclo*hex-1′-enyl-1-*p*-xylyl*cyclo*hexanol (19%) as a viscous liquid yielding a crystalline *epoxide*, m. p. 133—134° (Found: C, 80·3; H, 9·2. $C_{20}H_{26}O_2$ requires C, 80·0; H, 9·3%). Cyclisation of this epoxide gave a gum which, when crystallised from glacial acetic acid, sublimed ($10^{-2}$ mm.), and then twice crystallised from

ethanol, gave 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-*octahydro*-9 : 12-*dimethyltriphenylene* (50%), m. p. 123—124 (Found: C, 90·5; H, 9·5. $C_{20}H_{24}$ requires C, 90·9; H, 9·1%). Dehydrogenation of this material gave a hydrocarbon (5%), m. p. 176·5—177° (Found: C, 92·3; H, 7·7%).

1 : 2-*Benzochrysene.*—(*a*) The Grignard reagent from 1-bromonaphthalene (36 g.) and 2-*cyclo*hex-1′-enyl*cyclo*hexanone (31 g.), after reaction together and working up in the usual way, gave naphthalene (22·5 g.) and 2-cyclo*hex*-1′-*enyl*-1-α-*naphthyl*cyclo*hexanol* (17 g.), b. p. 160—161°/$10^{-2}$ mm., which very slowly solidified (Found: C, 86·1; H, 8·6. $C_{22}H_{26}O$ requires C, 86·3; H, 8·5%), m. p. 104—104·5° (from light petroleum). The crystalline *epoxide*, m. p. 159·5—160° (from ether–benzene) (Found: C, 82·0; H, 8·2. $C_{22}H_{26}O_2$ requires C, 82·0; H, 8·1%), was cyclised and the product was dehydrogenated. The resultant hydrocarbon was sublimed ($10^{-2}$ mm.) and crystallised from acetic acid, giving 1 : 2-benzochrysene, m. p. 115—115·5°; Bradsher and Rapoport [13] give m. p. 115—116°.

(*b*) An analogous experiment with 2-naphthylmagnesium bromide gave 2-cyclo*hex*-1′-*enyl*-1-β-*naphthyl*cyclo*hexanol* as a viscous oil (Found: C, 87·5; H, 8·4%) which yielded a crystalline *epoxide*, m. p. 164—164·5° (from ether–benzene) (Found: C, 82·0; H, 8·1%). This epoxide was cyclised, the product was dehydrogenated, and the resultant material was sublimed, giving a solid, m. p. 103—107°, which was readily separated by elution with benzene–light petroleum ether from an alumina column into 1 : 2-benzochrysene, m. p. 115°, and 1 : 2 : 3 : 4-dibenzanthracene, m. p. 205°; Clar [14] gives m. p. 205° for the latter compound.

*Cyclisation of* 2-(1 : 2-*Epoxy*cyclo*hexyl*)-1-o-*methoxy*cyclo*hexanol*.—o-Methoxyphenylmagnesium bromide and 2-*cyclo*hex-1′-enyl*cyclo*hexanone gave 2-cyclo*hex*-1′-*enyl*-1-o-*methoxyphenyl*-cyclo*hexanol*, b. p. 140—141°/$10^{-2}$ mm., prisms, m. p. 68—70° (Found: C, 79·5; H, 9·0. $C_{19}H_{26}O_2$ requires C, 79·7; H, 9·1%); Rapson [9] obtained this material in semisolid form and gave no analytical data. The derived *epoxide* had m. p. 137° (from ether–benzene) (Found: C, 75·2; H, 8·4. $C_{19}H_{26}O_3$ requires C, 75·5; H, 8·6%) and gave traces of triphenylene as the only crystalline product after cyclisation followed by dehydrogenation.

THE UNIVERSITY, HULL. [*Received, August 8th*, 1957.]

[13] Bradsher and Rapoport, *J. Amer. Chem. Soc.*, 1943, **65**, 1646.
[14] Clar, *Ber.*, 1929, **62**, 1574.

---

## 215. 5-*Methyl*-3 : 4-*benzofluorene.*

By B. R. T. KEENE and K. SCHOFIELD.

The Robinson–Mannich reaction has been used in syntheses of 6 : 7 : 8 : 13-tetrahydro-3 : 4-benzofluoren-6-one and its 5-methyl homologue. These were converted into 3 : 4-benzofluorene and 5-methyl-3 : 4-benzofluorene respectively.

FAILING to obtain 5-methyl-3 : 4-benzofluorene by a Bougault-type cyclisation, which provided a satisfactory means of obtaining some of its isomers,[1] we sought another route to this compound.

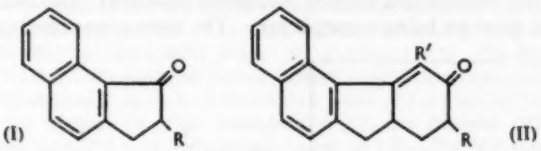
The Robinson–Mannich reaction, which has been applied to the synthesis of fluorene derivatives,[2] promised to be useful, and initially we examined its use in preparing 3 : 4-benzofluorene itself.

4 : 5-Benzindan-3-one was prepared by Ansell and Hey [3] on a very small scale by cyclising β-2-naphthylpropionic acid with hydrogen fluoride. We found this cyclisation to proceed smoothly and efficiently on the larger scale, and the product (I; R = H) reacted readily with paraformaldehyde and morpholine hydrochloride to give 2-morpholinomethyl-4 : 5-benzindan-3-one hydrochloride (I; R = $-CH_2 \cdot C_4H_8ON,HCl$). The free base, liberated in the cold from this sparingly soluble salt (heat caused decomposition), readily formed a quaternary salt with methyl iodide. The methiodide reacted

[1] Keene and Schofield, *J.*, 1957, 3181.
[2] Harradence and Lions, *J. Chem. Soc. New South Wales*, 1938, 284.
[3] Ansell and Hey, *J.*, 1950, 2874.

XUM

quickly with ethyl sodioacetoacetate, to give a moderately good yield of ethyl 6 : 7 : 8 : 13-tetrahydro-6-oxo-3 : 4-benzofluorene-7-carboxylate (II; R = $CO_2Et$, R′ = H). In the fluorene series Harradence and Lions [2] removed the ethoxycarbonyl group from the compound analogous to (II; R = $CO_2Et$, R′ = H) by heating it at 190° with glycerol containing 10% of water. With the compound (II; R = $CO_2Et$, R′ = H) this reagent gave only intractable tars, but hydrolysis and decarboxylation proceeded smoothly when the ester was boiled with 2N-hydrochloric acid in acetic acid.




(I) (II)

We failed to hydrogenate the resulting 6 : 7 : 8 : 13-tetrahydro-3 : 4-benzofluoren-6-one (II; R = R′ = H), and the amorphous solid formed on reduction with lithium aluminium hydride gave only tars when heated with palladised charcoal. However, the ketone was reduced cleanly by the Meerwein–Ponndorf procedure, with aluminium *iso*propoxide in propan-2-ol, and the resulting oily alcohol underwent dehydration and dehydrogenation when heated with palladised charcoal, giving 3 : 4-benzofluorene in reasonable yield.

To extend this variation of the method to the synthesis of 5-methyl-3 : 4-benzofluorene, we attempted to condense 2-morpholinomethyl-4 : 5-benzindan-3-one methiodide with ethyl sodio-β-oxovalerate. As in the previous case, the reaction solution quickly became red-brown, but no solid separated. Acidification and extraction isolated a brown oil from which no homogeneous product could be obtained directly. When it was heated with hydrochloric–acetic acid only a small quantity of 4 : 5-benzindan-3-one was recovered.

For an application of the alternative type of Robinson–Mannich synthesis, 4 : 5-benzindan-3-one was converted into 2-formyl-4 : 5-benzindan-3-one (I; R = CHO). This reacted with 4-piperidinobutan-2-one methiodide in absolute methanolic sodium methoxide, to give the crystalline diketone (I; R = $CH_2$·$CH_2$·COMe) in good yield, the formyl group being eliminated. When heated with a mixture of acetic and hydrochloric acid the diketone was converted into the tetracyclic compound (II; R = R′ = H).

In the same way, 1-diethylaminopentan-3-one methiodide reacted with 2-formyl-4 : 5-benzindan-3-one, to give the diketone (I; R = $CH_2$·$CH_2$·COEt), and acid cyclisation then produced the required 6 : 7 : 8 : 13-tetrahydro-5-methyl-3 : 4-benzofluoren-6-one (II; R = H, R′ = Me). The αβ-unsaturated ketones (II; R = H, R′ = H and Me severally) gave ultraviolet extinction curves [4] showing the expected [5] broad band in the 320—350 mμ region. Meerwein–Ponndorf reduction of the ketone (II; R = H, R′ = Me) under the conditions mentioned earlier, and subsequent dehydration and dehydrogenation, afforded 5-methyl-3 : 4-benzofluorene. The overall yield was considerably lower than in the case of the parent compound.

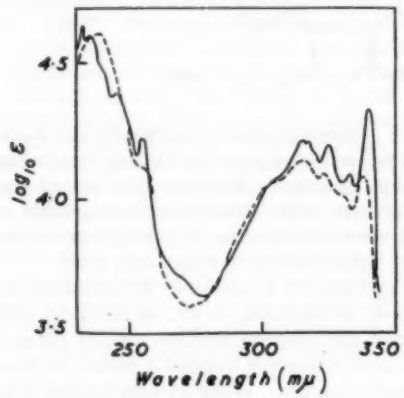
In the 3 : 4-benzophenanthrene series [6] the 5-methyl derivatives show abnormally high m. p.s, and in contrast to their isomers do not form picrates. The m. p. of 5-methyl-3 : 4-benzofluorene was not abnormal, and it did form a picrate. The latter, like others in this series, decomposed rapidly enough to make accurate analysis difficult. Clear evidence of molecular overcrowding in 5-methyl-3 : 4-benzofluorene was provided by its ultraviolet extinction curve. Compared with those of other methyl-3 : 4-benzofluorenes (see Figure) it showed a loss of fine structure and a decrease in the intensity of the three peaks in the 310—340 mμ range. These changes are characteristic of overcrowded

[4] Full curves for a number of compounds described in this paper and in ref. 1 are given by Keene, Ph.D. Thesis, 1957, Exeter University.
[5] Wilds, Beck, Close, Djerassi, Johnson, Johnson, and Shunk, *J. Amer. Chem. Soc.*, 1947, **69**, 1985.
[6] Newman and Wheatley, *ibid.*, 1948, **70**, 1913.

XUM

molecules and have been observed in 3 : 4-benzophenanthrenes,[6,7] chrysenes,[8] and 5 : 6-benzophenanthridines.[9]

Unexpected difficulties prevented the extension of these methods to the synthesis of naphtho(2' : 1'-3 : 4)fluorenes. 3'-Oxo-3 : 4-*cyclo*pentanophenanthrene[10] was conveniently prepared by cyclising β-3-phenanthrylpropionic acid with polyphosphoric acid (hydrogen fluoride produced a mixture of ketones, presumably by causing cyclisation in both possible directions), but we were unable to formylate this ketone. A number of attempts using ethyl formate and sodium methoxide produced only traces of alkali-soluble material, the main product being a purple tar. The ketone was unchanged by treatment




——— 7-*Methyl*-3 : 4-*benzofluorene* (*in* cyclo*hexane*).
*The curves for* 6- *and* 8-*methyl*-3 : 4-*benzofluorene were very similar.*[4]
– – – – 5-*Methyl*-3 : 4-*benzofluorene* (*in* cyclo*hexane*).

with diethyl carbonate and sodium hydride under a variety of conditions, and with paraformaldehyde and morpholine hydrochloride gave a poor yield of an unidentified substance.

## Experimental

4 : 5-*Benzindan*-3-*one*.—β-2-Naphthylpropionic acid (13·1 g.), set aside with hydrogen fluoride (130 g.) until most of the latter had evaporated, gave in the usual way the ketone (10·1 g.), m. p. 102—104° (un-recrystallised) (lit.,[11] m. p. 102—103°).

2-*Morpholinomethyl*-4 : 5-*benzindan*-3-*one*.—From a boiling solution of 4 : 5-benzindan-3-one (8 g.), morpholine hydrochloride (5·36 g.), and paraformaldehyde (1·45 g.) in absolute ethanol (10 c.c.), solid began to separate after 30 min. After 90 min. more of heating, the hydrochloride (13·0 g.), m. p. 203—205° (decomp.), was collected. A vigorously stirred suspension of this compound in water (750 c.c.) and ether (500 c.c.) was basified with 2N-sodium carbonate. When no solid remained the ether layer was separated, dried ($Na_2SO_4$), and evaporated. 2-*Morpholinomethyl*-4 : 5-*benzindan*-3-*one* (6·54 g.) formed needles, m. p. 127—128° (Found: C, 77·1; H, 6·9. $C_{18}H_{19}O_2N$ requires C, 76·8; H, 6·8%), from ethanol.

*Ethyl* 6 : 7 : 8 : 13-*Tetrahydro*-6-*oxo*-3 : 4-*benzofluorene*-7-*carboxylate*.—Crude 2-morpholinomethyl-4 : 5-benzindan-3-one (6·54 g.) and methyl iodide (15 ml.) were heated under reflux for 30 min., then set aside, with occasional shaking, for 30 min. more. Excess of methyl iodide was removed in a vacuum-desiccator, and the methiodide (m. p. 137—140°) was treated with a solution of ethyl sodioacetoacetate [from sodium (0·8 g.), ethyl acetoacetate (4·55 g.), and ethanol (25 c.c.)]. The mixture was heated under reflux for 2 hr., and the product (3·94 g.) was collected and washed with much warm water. The *ester* formed straw-coloured needles, m. p. 171—173° (Found: C, 78·3; H, 6·2. $C_{20}H_{18}O_3$ requires C, 78·4; H, 5·9%), from ethyl acetate.

6 : 7 : 8 : 13-*Tetrahydro*-3 : 4-*benzofluoren*-6-*one*.—(i) The keto-ester (2·63 g.), 2N-hydrochloric acid (120 c.c.), and acetic acid (180 c.c.) were heated under reflux for 6—7 hr. The

[7] Badger and Walker, *J.*, 1954, 3238.
[8] Jones, *J. Amer. Chem. Soc.*, 1941, **63**, 313.
[9] Mills and Schofield, *J.*, 1956, 4213.
[10] Bachmann and Kloetzel, *J. Amer. Chem. Soc.*, 1937, **59**, 2207.
[11] Cook and Hewett, *J.*, 1933, 1098.

solution was diluted with ice-water, and after 12 hr. the substantially pure product (1·32 g.) was collected. Straw-coloured plates of 6 : 7 : 8 : 13-*tetrahydro*-3 : 4-*benzofluoren*-6-*one*, m. p. 117—118° (Found: C, 87·0; H, 6·0. $C_{17}H_{14}O$ requires C, 87·15; H, 6·0%), $\lambda_{max.}$ 237, 251, 266, 321, 338, 352 mμ ($\log_{10}\varepsilon$ 4·44, 4·36, 4·02, 4·19, 4·18, 4·20 , separated from a small volume of ethyl acetate. The 2 : 4-*dinitrophenylhydrazone* formed dark-red needles, m. p. 250—260° (decomp.) (Found: C, 66·6; H, 4·3. $C_{23}H_{18}O_4N_4$ requires C, 66·7; H, 4·4%), from benzene.

(ii) 2-3′-Oxobutyl-4 : 5-benzindan-3-one (1·0 g.) (see below), acetic acid (25 c.c.), concentrated hydrochloric acid (15 c.c.), and water (7 c.c.) were heated under reflux, under nitrogen, for 3 hr. A benzene extract of the cooled, diluted solution was washed with sodium carbonate solution and evaporated. The residue was triturated with ethyl acetate–light petroleum (b. p. 60—80°), giving a solid (0·4 g.; m. p. 110—112°). The ketone formed yellow prisms, m. p. 117—118°, from aqueous dioxan, identical with the compound described above.

2-*Formyl*-4 : 5-*benzindan*-3-*one*.—4 : 5-Benzindan-3-one (9·1 g.) in dry benzene (80 c.c.) was added to an ice-cold mixture of ethyl formate (7·4 g.), dry benzene (80 c.c.), and sodium methoxide (prepared from 2·4 g. of sodium and baked at 180—200°/0·5 mm. for 1½ hr.). The mixture was set aside, with occasional shaking, for 1 hr. at room temperature, and then heated under reflux for 1 hr. The benzene extract of the diluted and acidified mixture was washed with water and with dilute aqueous potassium hydroxide. Acidification of the alkaline extract with 10% hydrochloric acid gave the substantially pure product (7·58 g.). 2-*Formyl*-4 : 5-*benzindan*-3-*one* formed clusters of biscuit-coloured needles, m. p. 170—172° (decomp.) (Found: C, 81·3; H, 4·7. $C_{14}H_{10}O_2$ requires C, 80·0; H, 4·8%), from ethyl acetate.

2-3′-*Oxobutyl*-4 : 5-*benzindan*-3-*one*.—4-Piperidinobutan-2-one (7·6 g.) [12] was treated gradually at 0°, with swirling and shaking, with methyl iodide (7·6 g.). After being kept at 0° for 2 hr. the mixture was allowed to reach room temperature and the product was washed by decantation with ether and then freed at reduced pressure from traces of this solvent. The methiodide in methanol (30 c.c.) was added to 2-formyl-4 : 5-benzindan-3-one (3·93 g.) in methanolic sodium methoxide [from sodium (0·43 g.) and methanol (30 c.c.)]. After 36 hr. the yellow solution was diluted with water and extracted with benzene. The brown oil (3·34 g.) from the dried ($Na_2SO_4$) extract crystallised when scratched. 2-3′-*Oxobutyl*-4 : 5-*benzindan*-3-*one* formed platelets, m. p. 64—65° (Found: C, 81·0; H, 6·3. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4%), from aqueous methanol.

3 : 4-*Benzofluorene*.—6 : 7 : 8 : 13-Tetrahydro-3 : 4-benzofluoren-6-one (0·5 g.), aluminium *iso*propoxide (1 g.), and absolute propan-2-ol (15 c.c.) were heated under reflux in such a way that the acetone produced distilled from the mixture. When acetone was no longer formed the propanol was removed and the residue was decomposed with ice-cold dilute hydrochloric acid. The yellow-brown gum (0·46 g.) obtained by benzene extraction did not crystallise. It was heated with 30% palladised charcoal (0·1 g.) at 240° in nitrogen for 1½ hr. Sublimation (120°/0·05 mm.) of the gum extracted by ether from the cooled reaction mixture gave 3 : 4-benzofluorene (0·13 g.), which formed flakes, m. p. 125—126°, from ethanol (lit.,[13] m. p. 124—125°).

2-3′-*Oxopentyl*-4 : 5-*benzindan*-3-*one*.—1-Diethylaminopentan-3-one methiodide [prepared from 1-diethylaminopentan-3-one (1·45 g.) [14] in the way described for the lower homologue] in methanol (10 c.c.) was added to 2-formyl-4 : 5-benzindan-3-one (1·05 g.) in methanolic sodium methoxide [from sodium (0·12 g.) and methanol (10 c.c.)]. After 24 hr. the solution was processed as before, giving 2-3′-*oxopentyl*-4 : 5-*benzindan*-3-*one* (0·99 g.) which formed needles, m. p. 54—55° (Found: C, 81·6; H, 7·4. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8%), from aqueous methanol.

6 : 7 : 8 : 13-*Tetrahydro*-5-*methyl*-3 : 4-*benzofluoren*-6-*one*.—The above diketone (0·9 g.), acetic acid (37·5 c.c.), concentrated hydrochloric acid (22·5 c.c.), and water (12 c.c.) were heated under reflux, under nitrogen, for 3 hr. Dilution and extraction with benzene recovered a brown oil which when triturated with methanol gave the product (0·41 g.). The *ketone* formed pale yellow tablets, m. p. 147—148° (Found: C, 86·2; H, 6·1. $C_{18}H_{16}O$ requires C, 87·1; H, 6·5%), $\lambda_{max.}$ 240, 269, 321, 337, 350 mμ ($\log_{10}\varepsilon$ 4·43, 3·97, 4·13, 4·12, 4·14), from methanol.

5-*Methyl*-3 : 4-*benzofluorene*.—The ketone (0·2 g.) was reduced with aluminium *iso*propoxide (1 g.) in propan-2-ol as described above. Similar processing gave a viscous yellow oil which

[12] Wilds and Werth, *J. Org. Chem.*, 1952, **17**, 1149.
[13] Cook, Dansi, Hewett, Iball, Mayneord, and Roe, *J.*, 1935, 1319.
[14] Adamson, McQuillin, Robinson, and Simonsen, *J.*, 1937, 1576.

was heated under nitrogen with 30% palladised charcoal, initially at 190°, rising to 240° in 30 min., and being maintained there for 15 min. Sublimation of the ether-soluble product (0·05 g.), and crystallisation from aqueous ethanol gave fibrous needles of *5-methyl-3 : 4-benzofluorene*, m. p. 85—86° (Found: C, 93·3; H, 6·3. $C_{18}H_{14}$ requires C, 93·9; H, 6·1%).

The picrate formed red needles, m. p. 130—131° (Found: C, 64·3; H, 4·1. Calc. for $C_{18}H_{14}.C_6H_3O_7N_3$: C, 62·7; H, 3·7%), from ethanol. Satisfactory analyses could not be obtained because of the fairly rapid decomposition of the compound.

β-3-*Phenanthrylpropionic Acid*.—β-3-Phenanthrylacrylic acid [10] (5 g.), 10% palladised strontium carbonate (0·5 g.), and dioxan (500 c.c.) were shaken with hydrogen until uptake ceased. Filtration, removal of the solvent, and trituration of the residue with benzene gave the acid (3·3 g.), m. p. 155—156° (lit.,[10] m. p. 158·5—159·5°).

3′-*Oxo*-3 : 4-cyclo*pentenophenanthrene*.—The above acid (0·5 g.) and polyphosphoric acid (20 g.) were stirred vigorously at 95—100° until a deep red solution was formed (*ca.* 1½ hr.). This was poured on ice, and the product was extracted with benzene. The ketone (0·37 g.) formed pale yellow needles, m. p. 139—141°, from aqueous acetic acid (lit.,[10] m. p. 142°).

The *oxime* gave yellow prisms, m. p. 222—223° (decomp.) (Found: C, 81·9; H, 4·9. $C_{17}H_{13}ON$ requires C, 82·6; H, 5·3%), from acetone–ethanol.

When the ketone (0·23 g.), morpholine hydrochloride (0·12 g.) and paraformaldehyde (0·03 g.) were boiled together in absolute ethanol (15 c.c.) for 3 hr. no solid separated. Removal of the solvent and trituration of the residue with ethanol gave a solid (0·19 g.), m. p. 164—165° (Found: C, 68·7; H, 6·15; N, 3·5%) after crystallisation from chloroform. It appeared to contain ionic chlorine.

THE UNIVERSITY, EXETER. [*Received, September 17th*, 1957.]

---

## 216. *Conductometric Investigation of the Rate of Hydrolysis of Nitriles in 100% Sulphuric Acid.*

By (MISS) M. LILER and DJ. KOSANOVIĆ.

The electrical conductivities of the solutions of acetonitrile and benzonitrile in 100% sulphuric acid at 25° decrease with time to a limiting value, owing to a decrease in the concentration of the highly mobile $HSO_4^-$ ions which results from the reactions, $RCN + 2H_2SO_4 = R{\cdot}CO{\cdot}NH_2 + H_2S_2O_7$ (1), or $R{\cdot}CNH^+ + HSO_4^- + H_2SO_4 = R{\cdot}CO{\cdot}NH_2^+ + HS_2O_7^-$ (2), with subsequent solvolysis of the $HS_2O_7^-$ ion. Calculation of the first-order reaction rate constants from the electrical conductivity changes gives values increasing with concentration. Second-order reaction rate constants, corresponding to equation (2), are calculated to be: acetonitrile, $k = 8{\cdot}01 \times 10^{-3}$ kg. mole$^{-1}$ min.$^{-1}$ (in the range 0·15—0·43 mole kg.$^{-1}$); benzonitrile, $k = 3{\cdot}54 \times 10^{-1}$ kg. mole$^{-1}$ min.$^{-1}$ (in the range 0·07—0·19 mole kg.$^{-1}$); both independent of concentration. A possible reaction mechanism is discussed.

On the basis of electrical conductivity values for $t = 0$, obtained by extrapolation, the degrees of dissociation and the basic dissociation constants for the two nitriles have been obtained: acetonitrile $K_b = 0{\cdot}157$; benzonitrile $K_b = 0{\cdot}076$.

THE only previous investigation of the behaviour of nitriles in sulphuric acid was made cryoscopically by Hantzsch [1] in 1909. He found that nitriles ionise as bases in sulphuric acid, the molecular weights obtained being about 70% of their normal values, in contrast to the majority of organic oxygen compounds, whose molecular weights in sulphuric acid he found to be about 50% of their normal values. On the basis of these results Hammett [2] classified nitriles as substances which are practically completely ionised in sulphuric acid,

[1] Hantzsch, *Z. phys. Chem.*, 1909, **65**, 41.
[2] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York and London, 1940, p. 47.

behaving as simple strong bases. This is probably the reason why the attention of later investigators in this field has been diverted from nitriles, and the fact which arises from Hantzsch's investigations, that the nitriles are *not* strong bases in sulphuric acid, like a number of organic oxygen compounds, remained obscured. The weaker basicity of nitriles than of most oxygen bases has however, been observed, recently in some other investigations also.[3] The aim of the present investigation was originally to show that conductometrically, as well as cryoscopically, it can be proved that the nitriles are weak bases in sulphuric acid. In view of Hantzsch's finding [1] that the nitriles are regenerated when their solutions in sulphuric acid are poured into water, we expected to obtain constant electrical conductivity values for these solutions. However, our preliminary experiments showed that the electrical conductivities of the solutions of acetonitrile in sulphuric acid decrease with time, reaching finally a limiting value, which means that nitriles undergo some chemical change in sulphuric acid at a measurable rate. We have assumed that this is hydrolysis represented by the equation:

$$RCN + 2H_2SO_4 = R{\cdot}CO{\cdot}NH_2 + H_2S_2O_7 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

with subsequent ionisation of both reaction products, or

$$R{\cdot}CNH^+ + HSO_4^- + H_2SO_4 = R{\cdot}CO{\cdot}NH_3^+ + HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

accompanied by the solvolysis of the $HS_2O_7^-$ ion. In the course of this reaction the concentration of highly conducting $HSO_4^-$ ions is reduced and the conductivity therefore decreases. A careful examination of the changes of electrical conductivity with time has shown that first-order, as well as second-order, reaction rate constants can be calculated from them.

The rate of hydrolysis of nitriles has hitherto been investigated only for aqueous solutions [4] where they give, first, amides, then acids. In dilute acid solutions hydrolysis of amides is several times faster than that of nitriles, whereas in concentrated acid solutions this relation is reversed. Amides can be obtained by dissolving nitriles in 96% sulphuric acid, which means that the amides are not hydrolysed in this medium (see, however, ref. 5). Previous investigations have shown that acetamide and benzamide in 100% sulphuric acid ionise as strong simple bases and remain otherwise unchanged.[6] Therefore the simplest nitriles—acetonitrile and benzonitrile—were chosen for these investigations.

The applicability of the conductometric method for following the kinetics of a reaction depends on whether or not the changes of electrical conductivity are a known function of the decreasing concentration of reactants and the increasing concentration of the products, the most favourable dependence being a linear one. It is well known that in dilute solutions of bases in sulphuric acid and in dilute oleum the changes of electrical conductivity with concentration of the dissolved bases or sulphur trioxide are approximately linear, except in the region of the minimum corresponding to 100% sulphuric acid, owing to the self-dissociation of sulphuric acid.[7] Since reactions (1) or (2) occur, however, at relatively considerable ionic concentrations in sulphuric acid, it is a reasonable assumption that the self-dissociation of sulphuric acid will not affect the linearity of electrical conductivity changes with concentration in the course of the reaction. In fact, the concentration-dependence of the initial and the final value of electrical conductivity of the solutions of acetonitrile (in the range of 0·15—0·43 mole kg.$^{-1}$) and of benzonitrile

[3] Lemaire and Lucas, *J. Amer. Chem. Soc.*, 1951, **73**, 5198; Pratt and Matsuda, *ibid.*, 1953, **75**, 3739; Tsubomura, *Bull. Chem. Soc. Japan*, 1954, **27**, 445.

[4] Krieble and Noll, *J. Amer. Chem. Soc.*, 1939, **61**, 560; Rabinovich, Winkler, and Stewart, *Canad. J. Res.*, 1942, **20**, *B*, 121; Rabinovich and Winkler, *ibid.*, p. 221; Remick, "Electronic Interpretations of Organic Chemistry," Chapman and Hall, Ltd., London, 1949, p. 422; Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1956, pp. 299—300.

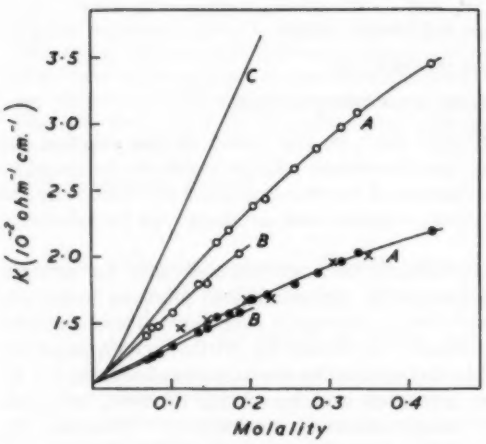
[5] Duffy and Leisten, *Nature*, 1956, **178**, 1242.

[6] Hantzsch, *Z. phys. Chem.*, 1907, **61**, 257; Oddo and Scandola, *Gazzetta*, 1909, **39**, I, 569; Tutundžić, Liler, and Kosanović, *Bull. Soc. chim. Beograd*, 1954, **19**, 225.

[7] Gillespie and Wasif, *J.*, 1953, 204.

(in the range of 0·07—0·19 mole kg.$^{-1}$) in sulphuric acid is approximately linear (Tables 3 and 4, p. 1088, and Figure). Therefore it is justifiable to use the changes of electrical conductivity with time to evaluate the changes of concentration of the nitriles in the course of the reaction.

We considered, however, that it was necessary to confirm the correctness of our assumption that the final values of electrical conductivities represent in fact the conductivities of amides in dilute oleum of equivalent concentration of sulphur trioxide. The first indication that this is so is that the solutions of benzonitrile, which is immiscible with water, give a layer of nitrile when poured into water 10—20 minutes after dissolution, but not after the completion of the reaction (when $\kappa_\infty$ is reached) in agreement with the solubility of the amide in water. It has been observed also that after completion of the reaction the solutions evolve much more sulphur trioxide vapour than does 100% sulphuric acid itself. Final evidence was obtained by measuring the electrical conductivity of




*Initial and final values of electrical conductivity of acetonitrile and benzonitrile in sulphuric acid.*

*A*, *Acetonitrile.*
*B*, *Benzonitrile.*
*C*, $KHSO_4$.
×, *Acetamide in dilute oleum.*
○, *Initial.*
●, *Final.*

solutions of acetamide in dilute oleum of equivalent trioxide concentration. The trioxide content of the dilute oleum was estimated on the basis of electrical-conductivity values of dilute oleum given by Gillespie and Wasif.[7] An equivalent quantity of the amide was then dissolved in a weighed quantity of the oleum, and the electrical conductivity was measured again. The results are given in Table 7 (p. 1090). It was found that the electrical conductivity of the oleum was lowered by dissolution of the amide, as expected, because the equilibrium

$$H_2SO_4 + H_2S_2O_7 \rightleftharpoons H_3SO_4^+ + HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

is replaced by

$$CH_3{\cdot}CO{\cdot}NH_2 + H_2S_2O_7 \rightleftharpoons CH_3{\cdot}CO{\cdot}NH_3^+ + HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad (4)$$

in which the ions of high mobility $H_3SO_4^+$ do not participate any more. The final conductivity is due to the solvolysis of $HS_2O_7^-$ ions:

$$HS_2O_7^- + H_2SO_4 \rightleftharpoons HSO_4^- + H_2S_2O_7 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

which gives a certain concentration of highly mobile $HSO_4^-$ ions.[8] The equilibrium (4) is very probably shifted completely to the right, because the amides are ionised as strong bases in sulphuric acid (Hantzsch, and Oddo and Scandola [6]) and should be surely even more so in the presence of the stronger pyrosulphuric acid. The values of the electrical conductivities of acetamide in dilute oleum of equivalent concentration are also shown

[8] Gillespie and Wasif, *J.*, 1953, 209.

in the Figure: within the limits of experimental error they correspond very well to the final values of electrical conductivity of the solutions of acetonitrile in sulphuric acid, which means that the final state is in fact a solution of the amide in dilute oleum. Similar conductometric evidence for the reaction of the acetic and benzoic anhydride in sulphuric acid was given by Flowers, Gillespie, and Wasif [9] by dissolving acetic acid and benzoic acid in dilute oleum.

In this way it has been proved that in 100% sulphuric acid solutions acetonitrile and benzonitrile undergo hydrolysis and that the rate constants calculated on the basis of electrical-conductivity changes represent the rate constants for hydrolysis of these nitriles in 100% sulphuric acid.

The results for the changes of electrical conductivity with time are given for two representative experiments with acetonitrile and benzonitrile in Tables 1 and 2. Since sulphuric acid is present in large excess, reaction (1) can be treated as a first-order reaction. The corresponding rate constants have been calculated from the equation

$$k_{\mathrm{I}} = \frac{2{\cdot}303}{t} \log \frac{a}{a-x} = \frac{2{\cdot}303}{t} \log \frac{\kappa_0 - \kappa_\infty}{\kappa_t - \kappa_\infty} \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

on the assumption that the conductivity decreases linearly with the concentration of the nitrile and that the total change of electrical conductivity in the course of the reaction

TABLE 1. *Rate of hydrolysis of acetonitrile in* 100% *sulphuric acid on the basis of conductivity data.*

$a_0 = 0{\cdot}3359$ mole kg.$^{-1}$, Temp. = 25°.

| $t$ (min.) | $\kappa_t$ ($10^{-2}$ ohm$^{-1}$ cm.$^{-1}$) | $10^2 k_{\mathrm{I}}$ (min.$^{-1}$) | [$HSO_4^-$] | $a_t$ | $\beta$ | $10^2 k_{\mathrm{II}}$ (kg. mole$^{-1}$ min.$^{-1}$) |
|---|---|---|---|---|---|---|
| 0 | (3·070) | — | 0·1690 | 0·336 | — | — |
| 10 | 2·957 | 1·02 | 0·1605 | 0·303 | 0·255 | 6·66 |
| 20 | 2·857 | 1·07 | 0·1525 | 0·271 | 0·253 | 6·61 |
| 30 | 2·770 | 1·08 | 0·1460 | 0·243 | 0·245 | 6·93 |
| 40 | 2·695 | 1·07 | 0·1400 | 0·219 | 0·246 | 7·05 |
| 50 | 2·627 | 1·06 | 0·1350 | 0·198 | 0·244 | 7·19 |
| 60 | 2·569 | 1·05 | 0·1300 | 0·179 | 0·246 | 7·12 |
| 71 | 2·513 | 1·04 | 0·1260 | 0·161 | 0·243 | 7·25 |
| ∞ | 2·011 | | | | | |
| | | $k_{\mathrm{I}}$ (mean) = $1{\cdot}06 \times 10^{-2}$ | | | | $k_{\mathrm{II}}$ (mean) = $6{\cdot}98 \times 10^{-2}$ |

TABLE 2. *Rate of hydrolysis of benzonitrile in* 100% *sulphuric acid on the basis of conductivity data.*

$a_0 = 0{\cdot}1420$ mole kg.$^{-1}$, Temp. = 25°.

| $t$ (min.) | $\kappa_t$ ($10^{-2}$ ohm$^{-1}$ cm.$^{-1}$) | $10^2 k_{\mathrm{I}}$ (min.$^{-1}$) | [$HSO_4^-$] | $a_t$ | $\beta$ | $10 k_{\mathrm{II}}$ (kg. mole$^{-1}$ min.$^{-1}$) |
|---|---|---|---|---|---|---|
| 0 | (1·790) | — | 0·0730 | 0·1420 | — | — |
| 10 | 1·727 | 2·02 | 0·0687 | 0·1160 | 0·166 | 2·95 |
| 20 | 1·669 | 2·16 | 0·0645 | 0·0920 | 0·170 | 3·18 |
| 31 | 1·611 | 2·37 | 0·0603 | 0·0681 | 0·172 | 3·62 |
| 40 | 1·582 | 2·32 | 0·0583 | 0·0560 | 0·171 | 3·62 |
| 50 | 1·558 | 2·24 | 0·0568 | 0·0463 | 0·169 | 3·55 |
| 60 | 1·533 | 2·29 | 0·0550 | 0·0359 | 0·170 | 3·73 |
| 70 | 1·514 | 2·31 | 0·0536 | 0·0281 | 0·170 | 3·82 |
| ∞ | 1·446 | | | | | |
| | | $k_{\mathrm{I}}$ (mean) = $2{\cdot}28 \times 10^{-2}$ | | | | $k_{\mathrm{II}}$ (mean) = $3{\cdot}50 \times 10^{-1}$ |

is proportional to the initial concentration of the nitrile. This assumption is approximately correct, as can be seen from the Figure. However, the first-order rate constants obtained show in most experiments a trend to decrease with time, and the mean values of the rate constants show a definite increase with the concentration of the nitrile (Tables 3 and

[9] Flowers, Gillespie, and Wasif, *J.*, 1956, 607.

4). This can be understood if the reaction is in fact a second-order one, as represented by equation (2).

TABLE 3. *The initial and final values of electrical conductivity and rate constants for solutions of acetonitrile.*

| $a_0$ (mole kg.$^{-1}$) | $\kappa_0$ ($10^{-2}$ ohm$^{-1}$ cm.$^{-1}$) | $\kappa_\infty$ | $10^2k_I$ (min.$^{-1}$) | $\beta$ | $10^2k_{II}$ (kg. mole$^{-1}$ min.$^{-1}$) |
|---|---|---|---|---|---|
| 0·1573 | 2·100 | 1·532 | 0·90 | 0·274 | 10·18 |
| 0·1722 | 2·191 | 1·561 | 0·88 | 0·278 | 9·90 |
| 0·2032 | 2·370 | 1·667 | 0·90 | 0·268 | 8·06 |
| 0·2206 | 2·425 | 1·706 | 1·00 | 0·250 | 7·48 |
| 0·2572 | 2·649 | 1·782 | 0·98 | 0·256 | 7·65 |
| 0·2840 | 2·800 | 1·858 | 1·04 | 0·256 | 7·62 |
| 0·3164 | 2·964 | 1·951 | 1·13 | 0·248 | 7·67 |
| 0·3359 | 3·070 | 2·011 | 1·06 | 0·246 | 6·98 |
| 0·4296 | 3·440 | 2·182 | 1·26 | 0·225 | 7·05 |

$k_{II}$ (mean) $= 8·01 \times 10^{-2}$

TABLE 4. *The initial and final values of electrical conductivity and rate constants for solutions of benzonitrile.*

| $a_0$ (mole kg.$^{-1}$) | $\kappa_0$ ($10^{-2}$ ohm$^{-1}$ cm.$^{-1}$) | $\kappa_\infty$ | $10^2k_I$ (min.$^{-1}$) | $\beta$ | $10k_{II}$ (kg. mole$^{-1}$ min.$^{-1}$) |
|---|---|---|---|---|---|
| 0·0708 | 1·400 | 1·218 | 1·48 | 0·184 | 3·48 |
| 0·0765 | 1·460 | 1·242 | 1·68 | 0·206 | 3·71 |
| 0·0845 | 1·470 | 1·260 | 1·78 | 0·174 | 3·82 |
| 0·1024 | 1·570 | 1·322 | 1·78 | 0·168 | 3·48 |
| 0·1358 | 1·780 | 1·420 | 2·12 | 0·187 | 3·43 |
| 0·1420 | 1·790 | 1·446 | 2·28 | 0·170 | 3·50 |
| 0·1876 | 2·012 | 1·569 | 2·64 | 0·173 | 3·36 |

$k_{II}$ (mean) $= 3·54 \times 10^{-1}$

Treatment of electrical conductivity changes in order to calculate the second-order constants has to take into account the fact that the $HS_2O_7^-$ ions formed in the reaction according to the equation (2) are solvolysed [equation (5)], regenerating in this way a certain amount of $HSO_4^-$ which has taken part in the reaction. This means that the change of $HSO_4^-$ concentration during the reaction is less than the corresponding change of the nitrile concentration. We have assumed that this change is proportional to the change of the nitrile concentration, the proportionality constant being less than unity. The rate of the reaction is then given by

$$dx/dt = k_{II}(a - x)(b - \beta x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where $(a - x) = a_t$ is the actual concentration of the nitrile, calculated as $a_0(\kappa_t - \kappa_\infty)/(\kappa_0 - \kappa_\infty)$, and $(b - \beta x) = [HSO_4^-]$ is the actual concentration of $HSO_4^-$ ions, calculated on the basis of electrical conductivity values, by taking the corresponding concentration $c_s$ of a strong base ($KHSO_4$[10]) and using the equation:

$$[HSO_4^-] = c_s/2 + \sqrt{(c_s^2/4 + K_{ap})}$$

where $K_{ap} = 2·2 \times 10^{-4}$ (25°) is the autoprotolysis constant of sulphuric acid (the procedure suggested by Gillespie and Solomons [11]); $x$ is the concentration of the amide formed, calculated as $a_0(\kappa_0 - \kappa_t)/(\kappa_0 - \kappa_\infty)$, and $\beta$ is the proportionality constant defined as $(b - [HSO_4^-])/x$. By integrating this differential equation (7) the values of the second-order rate constant can be obtained:

$$k_{II} = \frac{1}{t} \cdot \frac{1}{b - \beta a} \ln \frac{a(b - \beta x)}{b(a - x)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

In order to calculate $k_{II}$ the value of $\beta$ must be found. The values of $\beta$ for all the experiments proved to be reasonably constant, as can be seen from the Tables 1 and 2 for the

[10] Gillespie and Wasif, *J.*, 1953, 221.
[11] Gillespie and Solomons, *J.*, 1957, 1796.

two representative experiments. In this way the assumption made in deriving the differential equation (7) is justified and the integral equation (8) may be used to find the values of the rate constants. Whether the overall concentration or the concentration of the ionised nitrile is introduced in this equation does not make much difference. The degree of ionisation of the nitrile no doubt changes with the concentration and with the changes occurring in the solvent during the reaction, but these changes are probably not very substantial, since the nature of the medium does not change appreciably.

The results for the second-order rate constants are given for acetonitrile and benzonitrile in Tables 3 and 4 respectively. The values for the rate constants for the hydrolysis of acetonitrile decrease somewhat with concentration, whereas those for benzonitrile are very satisfactorily constant. We believe therefore that the conductometric method which we have described offers a simple means for the investigation of the hydrolysis of a number of nitriles in 100% sulphuric acid. This would give data for the elucidation of electronic effects in these reactions, which are at present not at all clear (cf. Hine [4]). The only condition for the applicability of the method to a given nitrile is that it does not react with sulphuric acid in any other way and that the amide which is formed remains unchanged in dilute oleum. This condition is probably fulfilled by most saturated aliphatic and aromatic nitriles, which may also be substituted by groups which do not react with sulphuric acid or show only simple basic ionisation. Investigation of the temperature coefficients of the rate of hydrolysis by the conductivity method should present no difficulties.

The fact that the second-order law is so well applicable to the nitrile hydrolysis in sulphuric acid suggests that the reaction probably proceeds by a bimolecular mechanism. The higher rate obtained for the hydrolysis of benzonitrile than of acetonitrile indicates that the rate-determining step is attack on positively charged carbon of the nitrile group by negative $HSO_4^-$ ions:

$$R{\cdot}C{\vdots}NH^+ + HSO_4^- = R{\cdot}CO{\cdot}NH_2 + SO_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

It is probable that the ionised nitrile reacts, because the structure of the nitrile $R{\cdot}C{\vdots}N \longleftrightarrow R{\cdot}C^+{:}N^-$ after ionisation has a definite excess of positive charge on the carbon $R{\cdot}C^+{:}NH$. The nature of the radical directly influences the donor ability of the nitrile, an aromatic radical causing, through its inductive influence, a higher positive charge on the carbon. The resonance transfer of the positive charge from the α-carbon atom to the benzene ring does not seem to be able to diminish this charge very much, since benzonitrile is a weaker base and reacts faster than acetonitrile. The $HSO_4^-$ ions are also likely to be more reactive than the $H_2SO_4$ molecules, since the negative charge on the oxygen atoms is greater. Owing to the high dielectric constant of sulphuric acid, long-range electrostatic attraction between the ionised nitrile molecules and $HSO_4^-$ ions is probably negligible, but the probability that a sulphuric acid molecule in the vicinity of the positive $R{\cdot}C{\vdots}NH^+$ ion will lose one of its protons increases with increasing $HSO_4^-$ ion concentration in the solution. This provides a possible explanation for the increase in the rate produced by increasing $HSO_4^-$ ion concentration, in spite of the fact that the sulphuric acid molecules are present at any given moment in large excess around the positive nitrile ions.

Finally, the values of electrical conductivity for $t = 0$ (Tables 5 and 6), which are electrical conductivities of the nitriles in sulphuric acid, give the conductometric confirmation of the cryoscopic results of Hantzsch.[1] The line *C* in the Figure represents the electrical conductivity of potassium hydrogen sulphate,[10] which according to cryoscopic investigations shows 100% basic ionisation.[12] It can be seen that the values of electrical conductivities of the nitriles are considerably lower, indicating that the nitriles are incompletely ionised as bases in sulphuric acid. Using the procedure described by Gillespie and Solomons,[11] we have calculated the degrees of dissociation and the basic dissociation constants of these two nitriles. The values obtained are given in Tables

[12] Gillespie, Hughes, and Ingold, *J.*, 1950, 2473.

TABLE 5. *Basic dissociation constant of acetonitrile in 100% sulphuric acid.*

| $a_0$ (mole kg.$^{-1}$) | $\kappa_0$ ($10^{-2}$ ohm$^{-1}$ cm.$^{-1}$) | $\alpha$ | $K_b$ | $a_0$ (mole kg.$^{-1}$) | $\kappa_0$ ($10^{-2}$ ohm$^{-1}$ cm.$^{-1}$) | $\alpha$ | $K_b$ |
|---|---|---|---|---|---|---|---|
| 0·1573 | 2·100 | 0·598 | 0·143 | 0·2840 | 2·800 | 0·524 | 0·165 |
| 0·1722 | 2·191 | 0·587 | 0·147 | 0·3164 | 2·964 | 0·507 | 0·166 |
| 0·2032 | 2·370 | 0·567 | 0·153 | 0·3359 | 3·070 | 0·502 | 0·171 |
| 0·2206 | 2·425 | 0·542 | 0·143 | 0·4296 | 3·440 | 0·461 | 0·170 |
| 0·2572 | 2·649 | 0·533 | 0·158 | | | | |

$K_b$ (mean) = 0·157 ± 0·014

TABLE 6. *Basic dissociation constant of benzonitrile in 100% sulphuric acid.*

| $a_0$ (mole kg.$^{-1}$) | $\kappa_0$ ($10^{-2}$ ohm$^{-1}$ cm.$^{-1}$) | $\alpha$ | $K_b$ | $a_0$ (mole kg.$^{-1}$) | $\kappa_0$ ($10^{-2}$ ohm$^{-1}$ cm.$^{-1}$) | $\alpha$ | $K_b$ |
|---|---|---|---|---|---|---|---|
| 0·0708 | 1·400 | 0·579 | 0·0630 | 0·1358 | 1·780 | 0·508 | 0·0744 |
| 0·0765 | 1·460 | 0·595 | 0·0734 | 0·1420 | 1·790 | 0·493 | 0·0710 |
| 0·0845 | 1·470 | 0·545 | 0·0604 | 0·1876 | 2·012 | 0·464 | 0·0774 |
| 0·1024 | 1·570 | 0·527 | 0·0644 | | | | |

$K_b$ (mean) = 0·069 ± 0·009

TABLE 7. *Electrical conductivity of solutions of acetamide in dilute oleum of equivalent concentration.*

| | | | | | | |
|---|---|---|---|---|---|---|
| $\kappa$ (oleum) ($10^{-2}$ ohm$^{-1}$ cm.$^{-1}$) ..... | 1·520 | 1·681 | 1·864 | 1·966 | 2·211 | 2·306 |
| Concn. (mole kg.$^{-1}$) ..... | 0·112 | 0·145 | 0·195 | 0·226 | 0·305 | 0·350 |
| $\kappa$ (amide in oleum) ($10^{-2}$ ohm$^{-1}$ cm.$^{-1}$) | 1·457 | 1·521 | 1·668 | 1·678 | 1·949 | 1·996 |

5 and 6. The basic dissociation constants of the two nitriles are reasonably constant and are comparable in magnitude with those of nitrotoluenes.[11]

## EXPERIMENTAL

*Materials.*—Sulphuric acid was prepared according to Kendall and Carpenter.[13] Its m. p. was 10·4° and $\kappa_{25}$ was 1·05 × $10^{-2}$ ohm$^{-1}$ cm.$^{-1}$.

*Acetonitrile.* A " B.D.H. laboratory reagent " was treated with phosphoric oxide and then distilled. It had m. p. −41°, $d_4^{25}$ 0·7768.[14, 15]

*Benzonitrile.* A product from Dr. Fraenkel and Dr. Landau, Berlin, of m. p. −13·3°,[15] was not purified.

*Acetamide.* Material from E. Merck, Darmstadt, was recrystallised from benzene, then having m. p. 80·0°.

*Method.*—The measurements of electrical conductivity were carried out as previously described.[16] The solutions were prepared in the following way. Sulphuric acid (usually 15—20 g.) was weighed into a small glass-stoppered bottle, which was then kept in a water-thermostat at 25° ± 0·05° together with the empty electrical conductivity cell. After about 15 min. the bottle was taken out, and its weight quickly checked. The desired quantity of the nitrile was then added from a 1 ml. pipette, the mixture shaken, and the zero time noted. The bottle was then weighed again, and the mixture immediately poured into the conductivity cell in the thermostat. The whole procedure of preparing the solution lasted usually not more than 3—4 min. Electrical conductivity was measured after 10 min., then at 10 min. intervals. Values of electrical conductivity for $t = 0$ were found by graphical and numerical extrapolation of the curves. The final values of electrical conductivity were measured after 24 hr. and remained afterwards unchanged. Since the work was performed with relatively small quantities of sulphuric acid and the addition of the nitriles was made with an ordinary pipette, it is possible that the exclusion of moisture was not perfect in some experiments, which would account for the variations of the conductivity values themselves as well as of the reaction rate constants.

We thank Dr. R. J. Gillespie (University College, London) for useful discussion and help and Dr. J. A. Leisten (The University, Sheffield) for his comments.

INSTITUTE OF CHEMISTRY, BELGRADE, YUGOSLAVIA. [*Received, September 9th*, 1957.]

[13] Kendall and Carpenter, *J. Amer. Chem. Soc.*, 1914, **36**, 2498.
[14] Beilstein's " Handbuch der organischen Chemie," Bd. II, Springer Verlag, Berlin, 1920.
[15] Timmermans, " Physico-chemical Constants of Pure Organic Compounds," Elsevier Publ. Co., Amsterdam, 1950.
[16] Tutundžić and Liler, *Bull. Soc. chim. Beograd*, 1953, **18**, 521.

XUM

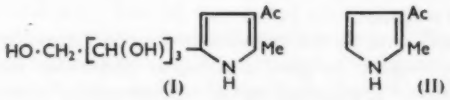
## 217. *Identification of Two Chromogens in the Elson–Morgan Determination of Hexosamines. A New Synthesis of 3-Methylpyrrole. Structure of the "Pyrrolene-phthalides."*

By J. W. Cornforth and (Mrs.) M. E. Firth.

The substance producing most of the colour with Ehrlich's reagent in the Elson–Morgan assay of hexosamines is shown to be 2-methylpyrrole; 3-acetyl-2-methylpyrrole is also formed. A synthesis of 3-methylpyrrole in four steps from 2-methylallyl chloride is described. Infrared spectra indicate that the condensation products of pyrroles with phthalic anhydride are benzo-[*f*]pyrrocoline-5 : 10-diones; several of these are described.

During the quarter-century which has elapsed since Elson and Morgan [1] published their method for the colorimetric determination of hexosamines, several modifications have increased its precision and specificity and have confirmed it as the method of choice for biochemical work; but in essence the procedure has not changed: the hexosamine is heated with acetylacetone in alkaline solution, and a purple-red colour is then generated by addition of Ehrlich's *p*-dimethylaminobenzaldehyde reagent.

Elson and Morgan assumed that glucosamine and acetylacetone condensed to yield 3-acetyl-2-methyl-5-(tetrahydroxybutyl)pyrrole (I) and that this substance reacts with *p*-dimethylaminobenzaldehyde, as pyrroles were known to do, to give the coloured product. Earlier, Pauly and Ludwig [2] condensed glucosamine with acetylacetone in concentrated alcoholic solution and obtained a crystalline product containing the pyrrole (I). Boyer and Furth [3] prepared the pure substance, showed that it gave a red colour with Ehrlich's reagent, and obtained evidence that the tetrahydroxybutyl group was absent from the coloured product.




The view that the trisubstituted pyrrole (I) is the chromogen was not challenged until 1951, when Schloss reported that a chromogen volatile with steam was formed in the initial reaction. On concentration of the alkaline liquid at low pressure and separate treatment of distillate and residual liquid with Ehrlich's reagent, the distillate gave a purplish-red solution absorbing maximally at 550 mμ and the residue an orange-red solution showing maximal absorption at 512 mμ. The volatile chromogen, Schloss reported, was unstable; he could not purify or identify it. From the non-volatile residue several fractions were prepared; of these, only one was both crystalline and chromogenic, and it was obtained in quantity too small for purification and analysis. Schloss concluded however that certainly two and probably three chromogens were present in the residue.

We succeeded in isolating the volatile chromogen from the distillate by way of an insoluble mercury complex and in purifying it by distillation at room temperature through magnesium perchlorate; later, a simpler isolation procedure was found. The general properties (including rapid oxidation in air) were suggestive of a pyrrole, and analysis indicated the formula $C_5H_7N$, which is that of a methylpyrrole. Condensation with phthalic anhydride gave a "phthalide" melting at 174°. Since the "phthalide" from 3-methylpyrrole was reported in Fischer and Orth's monograph [5] to melt at 157° whereas

[1] Elson and Morgan, *Biochem. J.*, 1933, **27**, 1824.
[2] Pauly and Ludwig, *Z. physiol. Chem.*, 1922, **121**, 176.
[3] Boyer and Furth, *Biochem. Z.*, 1935, **282**, 242.
[4] Schloss, *Anal. Chem.*, 1951, **23**, 1321.
[5] H. Fischer and Orth, "Die Chemie des Pyrrols," F. Enke, Stuttgart, 1933.

that from 2-methylpyrrole was given m. p. 215°, it was decided to prepare 3-methylpyrrole first for comparison; and the unsatisfactory nature of the known methods of synthesis prompted the development of a new process (see below). This pyrrole with phthalic anhydride gave two isomeric " phthalides," m. p. 223° and 169—170°. Mixture with the derivative from glucosamine did not depress the melting point of the more fusible compound; however, the infrared spectra of all three " phthalides " were different. A specimen of 2-methylpyrrole was then prepared by a ready Huang-Minlon reduction of the readily accessible [6] pyrrole-2-aldehyde. Its infrared spectrum was identical with that of the pyrrole from glucosamine and the melting points and infrared spectra of the derived " phthalides " were also identical. The melting points given in Fischer and Orth's monograph [5] should be transposed: the substances m. p. 215° and 157° were prepared by Dennstedt and Zimmermann [7] from 3-methylpyrrole and 2-methylpyrrole respectively.

For isolation of 2-methylpyrrole from the glucosamine–acetylacetone reaction, the glucosamine concentration was several hundred-fold higher than is used analytically. To test the importance of 2-methylpyrrole as a chromogen at concentrations customary in analysis, a reaction mixture prepared according to a good analytical procedure [8] was concentrated at low pressure. Distillate and residual liquid were each diluted to the original volume of the reaction mixture, and the colours developed by Ehrlich's reagent were compared with the colours from samples of the original reaction mixture and of dilute aqueous solutions of 2-methylpyrrole. This experiment showed that when the colour in an Elson–Morgan analysis is read, as is customary, at 530 mμ, somewhat more than two-thirds of the light absorption is derived from a chromogen readily volatile with steam and giving with Ehrlich's reagent a colour indistinguishable from that given by 2-methylpyrrole. The results leave little doubt that this pyrrole is the principal chromogen in the Elson–Morgan analysis; the computed yield is around 10% of the theoretical. Incidentally, 2-methylpyrrole at a concentration of 0·1 p.p.m. in aqueous ethanol is easily detectable by Ehrlich's reagent.

Schloss [4] produced evidence for the presence of a second chromogen which reacted very slowly with Ehrlich's reagent to give a solution absorbing maximally at 512 mμ. Anastassiadis and Common [9] found that higher concentrations of acetylacetone suppressed formation of this chromogen; its nature remains unknown, but it can make little contribution to colour production during the customary short period of incubation with Ehrlich's reagent.

The presence of another chromogen in the reaction mixture was indicated by Dr. A. Gottschalk (Melbourne), who found in 1955 (personal communication) that condensation of alkaline acetylacetone and glucosamine followed by chromatography on paper with butanol–acetic acid gave a single purple spot of $R_F$ 0·87 after spraying with Ehrlich's reagent and heating. The initial concentration of glucosamine was 10—20 times the usual analytical concentration. The material of $R_F$ 0·87 was not detectable on paper by Schiff's reagent after treatment with periodate. When the reaction mixture was extracted by ether and the extract was concentrated, a little crystalline, Ehrlich-positive material was obtained which absorbed maximally at 245 mμ and on chromatography gave the purple spot of $R_F$ 0·87. When the reaction mixture was concentrated at low pressure before chromatography, four weak spots of $R_F$ 0·80, 0·67, 0·58, and 0·48 respectively appeared along with the spot of $R_F$ 0·87 on spraying with Ehrlich's reagent.

Following this indication we extracted with ether the solution remaining after concentration of an Elson–Morgan reaction mixture. From the extract a crystalline substance was obtained which slowly gave a blue-purple colour ($\lambda_{max.}$ 570 mμ) with Ehrlich's reagent.

[6] Silverstein, Ryskiewicz, Willard, and Koehler, *J. Org. Chem.*, 1955, **20**, 668.
[7] Dennstedt and Zimmermann, *Ber.*, 1886, **19**, 2200.
[8] Nilsson, *Biochem. Z.*, 1936, **285**, 386.
[9] Anastassiadis and Common, *Canad. J. Chem.*, 1953, **31**, 1093.

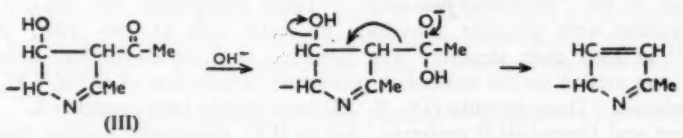
XUM

The empirical formula, $C_7H_9ON$, indicated that the substance was 3-acetyl-2-methylpyrrole (II), a structure which Dr. Gottschalk had predicted, on the basis of his observations, for the substance of $R_F$ 0·87, and which we confirmed by preparation of an identical substance by a Knorr synthesis from aminoacetaldehyde and acetylacetone. Dr. Gottschalk, to whom we are much indebted for communication and discussion of his results, found the material from both sources to have the expected $R_F$ 0·87 in butanol–acetic acid.

3-Acetyl-2-methylpyrrole is presumably formed from glucosamine and acetylacetone even at analytical concentrations of glucosamine, and since it reacts with Ehrlich's reagent it can be regarded as a chromogen. However, quantitative tests showed that the colour produced under analytical conditions was several hundred times fainter than the colour from an equimolar amount of 2-methylpyrrole. Since the yield of 3-acetyl-2-methylpyrrole cannot be even ten times that (10%) of the 2-methylpyrrole formed in the glucosamine–acetylacetone reaction, it seems that no significant proportion of the colour in an Elson–Morgan analysis originates from 3-acetyl-2-methylpyrrole.

The results of paper chromatography, which point to 3-acetyl-2-methylpyrrole as the principal chromogen, are in apparent conflict with the evidence assigning that position to 2-methylpyrrole. However, 2-methylpyrrole would have been lost by evaporation from the paper before it was sprayed with Ehrlich's reagent. The remarkably intense spot given by 3-acetyl-2-methylpyrrole on paper, contrasting with its feeble chromogenic power in solution, is explicable if the strongly acidic environment built up on heating the sprayed paper caused some deacetylation [10] to the intensely chromogenic 2-methylpyrrole.

When 2-methylpyrrole is formed from glucosamine and acetylacetone, a tetrahydroxybutyl group is lost at some stage from the glucosamine moiety and an acetyl group from the acetylacetone moiety. The fission between $C_{(2)}$ and $C_{(3)}$ of the glucosamine chain, which also occurs during formation of 3-acetyl-2-methylpyrrole, will be discussed elsewhere in a more general context: it can be formulated in several ways, each essentially of the retroaldol type. Theoretically, loss of the acetyl group might have occurred from a pyrrole, from acetylacetone, or from some intermediate stage. The first two explanations are untenable; 3-acetyl-4-methylpyrrole,[11] for example, withstands 10% aqueous sodium hydroxide at 140°, and it was easily shown that 3-acetyl-2-methylpyrrole was not converted into the intensely chromogenic 2-methylpyrrole by heat at pH 9—10, as in an Elson–Morgan reaction mixture. Again, when acetone was substituted for acetylacetone in an Elson–Morgan analysis, the colour formed on addition of Ehrlich's reagent was very weak. The acetyl group must therefore be lost at an intermediate stage. Addition of hydroxyl ion to an intermediate such as (III) may initiate a concerted elimination as shown.



(III)

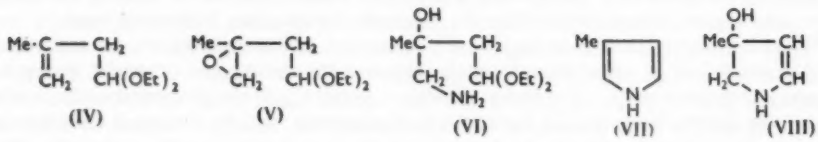
*Synthesis of 3-Methylpyrrole.*—4-Ethoxycarbonyl-3-methylpyrrole-5-carboxylic acid can be made in very poor yield [12] by a Knorr condensation of aminoacetone with ethyl oxaloacetate; the acid, when heated with concentrated aqueous potassium hydroxide, gives 3-methylpyrrole.[13] This appears to be the least inconvenient method hitherto described for preparing 3-methylpyrrole.

In the first step of the present synthesis, 2-methylallylmagnesium chloride reacts with

[10] H. Fischer and Bartholomäus, *Z. physiol. Chem.*, 1912, **80**, 6.
[11] H. Fischer, Sturm, and Friedrich, *Annalen*, 1928, **461**, 259.
[12] Piloty and Hirsch, *ibid.*, 1913, **395**, 70.
[13] H. Fischer and Rose, *ibid.*, 1935, **519**, 22.

ethyl orthoformate to form 3-methylbut-3-enal diethyl acetal (IV). This reaction gave Kritchevsky [14] a low yield of a product for which no analysis was given. From the data now available it can be estimated that this product contained about 25% of ethyl orthoformate. Our experience of Kritchevsky's procedure confirmed the low yield and the difficulty of purifying the product. Eventually the expedient of adding methylallyl chloride slowly to a stirred mixture of ethyl orthoformate and magnesium, in which reaction had been initiated by methyl iodide, gave a 54% yield of the acetal (IV). The purification was simplified by finding conditions, which did not affect the acetal, for hydrolysis of residual orthoformate. In a normal Tschitschibabin–Bodroux synthesis the Grignard reagent is prepared in ether, the orthoformate is added, and prolonged heating is required to complete the formation of acetal. In the present modification, ethyl orthoformate must participate as an ether in formation of the Grignard complex. The acetal may then be produced by an intramolecular reaction; if not, the high concentration of orthoformate seems at least to suppress the usually dominant side-reaction of the Grignard reagent with methylallyl chloride. In contrast, no improvement on Kritchevsky's yield was secured by adding methylallyl chloride to magnesium and ethyl orthoformate in dilute ethereal solution.

The unsaturated acetal reacted with perbenzoic or, better, with perphthalic acid to give the epoxide (V) in good yield. When this was treated with aqueous or methanolic ammonia the hydroxy-amino-acetal (VI) was formed; the postulated direction of addition



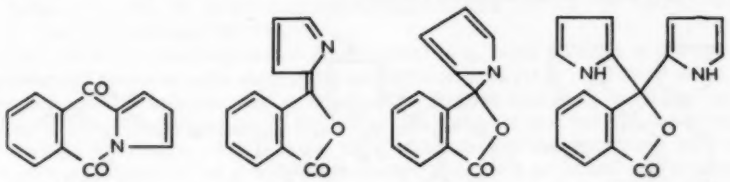

of ammonia is supported by well-known analogies and confirmed by what follows. When the acetal was dissolved in aqueous citric acid and distilled in steam, 3-methylpyrrole (VII) was isolated from the distillate in 39% yield. Probably the amino-aldehyde formed by acid hydrolysis of the acetal (VI) cyclises first to a hydroxypyrroline (VIII), which can be regarded as an intermediate in a hypothetical Knorr condensation of aminoacetone with acetaldehyde: it is presumed to give the pyrrole (VII) by spontaneous or acid-catalysed dehydration. The pyrrole is thus obtained in four stages from commercially available materials. Since large amounts of the final product were not required the last two stages were studied less extensively and conditions giving the best yields have probably not been found.

*Structure of the "Pyrrolene-phthalides."*—These compounds are usually made by heating pyrroles with phthalic anhydride in acetic acid at 180—190°. After their discovery [15] in 1884 their structure was discussed at intervals for half a century and eventually was settled to the somewhat premature satisfaction of Oddo,[16] H. Fischer,[17] and their schools. Three formulæ (IX, X, XI) have chiefly been considered.

Ciamician and Dennstedt [15] preferred (XI) to (IX), principally because they failed to induce reaction with hydroxylamine and V. Meyer [18] had had similar failures with known lactones. Ciamician [19] later preferred structure (X). Oddo [15] favoured (X) because he could obtain "pyrrolene-phthalide" by boiling pyrrophthalein (presumably XII) with hydrochloric acid, and he regarded this as evidence that both compounds have a lactone ring, though he recognised that this ring was probably broken at an early stage of the

[14] Kritchevsky, *J. Amer. Chem. Soc.*, 1943, **65**, 487.
[15] Ciamician and Dennstedt, *Ber.*, 1884, **17**, 2957.
[16] Oddo, *Gazzetta*, 1925, **55**, 242.
[17] H. Fischer and Orth, *Annalen*, 1933, **502**, 238.
[18] V. Meyer, *Ber.*, 1883, **16**, 1781; 1884, **17**, 817.
[19] Ciamician, *Ber.*, 1904, **37**, 4239.

reaction. Fischer and Orth [17] preferred (X) because " pyrrolene-phthalides " are yellow. None of these arguments appears impressive by modern standards: in particular a yellow colour, though decisive against (XI), is to be expected in a compound of classical structure (IX) in which quinonoid states (*e.g.*, XIII) must participate. Infrared spectrometry provides a crucial test. Grove and Willis [20] found the C=O stretching frequency of 3-methylenephthalide at 1780 cm.$^{-1}$; in phthalylideneacetic acid (XIV),



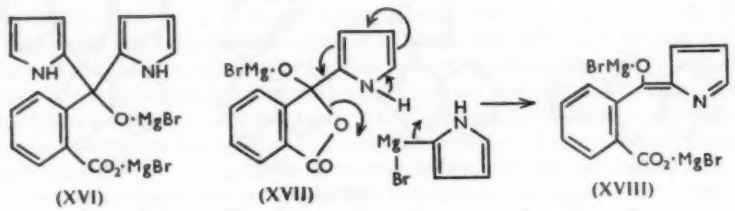

probably a closer model for (X), the stretching frequency of the lactone C=O was at 1800 cm.$^{-1}$. Thus if structure (X) is correct, " pyrrolene-phthalides " should absorb strongly near 1800 cm.$^{-1}$; if structure (IX) is correct the spectra should show the amide I band near 1700 cm.$^{-1}$ (cf. the Raman spectrum of 1-acetylpyrrole,[21] where the C=O stretching frequency is at 1716 cm.$^{-1}$), and a band near 1650 cm.$^{-1}$ due to the other carbonyl group (the C=O absorption of pyrrole-2-aldehyde, measured in dilute solution to reduce intermolecular hydrogen-bonding, was found at 1660 cm.$^{-1}$; cf. also the Raman spectrum of 2-acetylpyrrole [21]). In fact, no absorption near 1800 cm.$^{-1}$ was observed in our " pyrrolene-phthalides," which all showed a strong band at 1705—1708 cm.$^{-1}$ and another at 1650—1655 cm.$^{-1}$. This finding is consistent only with structure (IX); the " pyrrolene-phthalides " are therefore benzo[*f*]pyrrocoline-5 : 10-diones. The ultraviolet absorption of 1 : 3-dimethylbenzo[*f*]pyrrocoline-5 : 10-dione, incidentally, resembles that of many anthraquinones.

The stability and crystallising power of benzopyrrocolinediones makes them useful, as Fischer and Orth [5] have remarked, for characterising the simpler pyrroles. The poor yields of the reaction with phthalic anhydride are offset by a simple and effective technique of isolation described in the Experimental section. As indicated earlier, mixed melting points are not always reliable means of identification, but the infrared spectra are characteristic and rich in detail. The two isomerides from 3-methylpyrrole were easily separated by crystallisation.

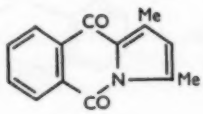
Ingraffia [22] reported the formation in small quantity of a *colourless* substance, which he formulated as the dimethyl analogue of (X), from the reaction of 2 : 4-dimethylpyrrylmagnesium bromide with phthalic anhydride. By a similar process with pyrrylmagnesium bromide, Oddo and Mingioia [23] had obtained traces of the yellow " pyrrolene-phthalide." The main product of each reaction was an oxo-acid (XV; R = H or Me). On repeating Ingraffia's experiment we obtained a colourless product which proved to be a magnesium salt of the acid (XV; R = Me); the earlier observation was presumably in error. The stoicheiometry of the Grignard reaction is of some interest, for Oddo and Mingioia reported

[20] Grove and Willis, *J.*, 1951, 877.
[21] Bonino and Chiorboli, *Atti Accad. naz. Lincei, Rend. Classe sci. fis., mat. nat.*, 1951, **10**, 104.
[22] Ingraffia, *Gazzetta*, 1934, **64**, 714.
[23] Oddo and Mingioia, *ibid.*, 1925, **55**, 235.

that about half the phthalic anhydride was recovered when equimolar amounts of the reactants were taken; yet when two equivalents of pyrrole to one of phthalic anhydride were used, about half the pyrrole was recovered. Oddo suggested that the first product of the reaction is (XVI) and that this loses pyrrole at an unspecified stage, but a more likely explanation is that the initial adduct (XVII) donates a proton to a second equivalent of pyrrylmagnesium bromide (the process is not necessarily cyclic as depicted here) to give the enolate (XVIII) which would react no further.




(XVI) (XVII) (XVIII)




(XIX)

The oxo-acid (XV; R = Me) was converted into the benzopyrrocolinedione (XIX) by the known technique[15] of heating it with slightly ammoniacal water. This benzopyrrocolinedione was identical with a specimen prepared directly from 2 : 4-dimethylpyrrole and phthalic anhydride. On mild alkaline hydrolysis the oxo-acid (XV; R = $CH_3$) was regenerated (cf. ref. 15).

## Experimental

M. p.s marked (K) were taken on a Kofler block and are corrected.

*2-Methylpyrrole and 3-Acetyl-2-methylpyrrole from Glucosamine.*—An aqueous solution (800 ml.) of D-glucosamine hydrochloride (21·6 g.) was added to an aqueous solution (2200 ml.) containing sodium carbonate (106 g.), acetylacetone (19·6 ml.; redistilled, b. p. 66—67°/80 mm.) and N-hydrochloric acid (200 ml.). The mixture (pH 9·75) in two portions was heated on steam-baths under reflux condensers. Heating was continued for 20 min. after the temperature became steady. The deep orange solutions were cooled below 30°, combined, and distilled at 20 mm. (bath 50°; receiver cooled in ice-salt), until the distillate gave no significant colour with Ehrlich's reagent (0·5 g. of *p*-dimethylaminobenzaldehyde in 20 ml. of ethanol and 5 ml. of concentrated hydrochloric acid).

The distillate (450 ml.) was saturated with salt and extracted with ether (6 × 40 ml.), which was then shaken once with 2N-sodium hydroxide and once with water. The combined aqueous and alkaline extracts were re-extracted with ether (2 × 10 ml.). The combined ethereal solutions were dried ($CaCl_2$) at 0° under nitrogen and evaporated at −10°/30—40 mm. The residue was distilled twice at room temperature and 1 mm. pressure, the vapour passing over magnesium perchlorate and condensing in a bulb at −70°. The product (650 mg., 8%) was a clear colourless mobile liquid (Found: C, 73·9; H, 8·7; N, 17·4. Calc. for $C_5H_7N$: C, 74·1; H, 8·6; N, 17·3%), b. p. 138—146°/766 mm. when distilled in a nitrogen atmosphere from a small flask. The product remained colourless in nitrogen at −5° but darkened rapidly in air. The infrared spectrum was identical with that of authentic 2-methylpyrrole (see below).

The residual liquids after collection of aqueous distillate from two runs were combined and heated on a steam-bath for 45 min., then distilled as before. The pyrrole was precipitated as a mercury complex by adding hot saturated aqueous mercuric chloride to the distillate. The solid was suspended in N-sodium hydrogen carbonate and decomposed by hydrogen sulphide. The product was extracted with ether and purified as above, to give 2-methylpyrrole (40 mg.) (Found: N, 17·2%). The infrared spectrum was identical with that of the main product.

XUM

The aqueous reaction mixture from which 2-methylpyrrole had been distilled was extracted continuously with ether for 24 hr. The product (*ca.* 1 g.) remaining after evaporation of ether under nitrogen was distilled at 0·6—0·7 mm. The partly solid distillate (b. p. ~110—115°) was sublimed at <100°/0·5 mm. The somewhat oily sublimate was suspended in 1 : 1 ether–light petroleum (b. p. 40—60°) and dry ether was added until the undissolved material was wholly crystalline. The collected solid (130 mg.) had m. p. 93—94° (K). Recrystallisation from light petroleum (b. p. 60—80°) gave white needles, m. p. 94—95° (K), of 3-*acetyl-2-methylpyrrole* (II) (Found: C, 68·4; H, 7·2; N, 11·5. $C_7H_9ON$ requires C, 68·3; H, 7·3; N, 11·4%), ν (in KCl) 1620 cm.$^{-1}$, ν (in $CCl_4$) 1660 cm.$^{-1}$ (C=O).

*Synthesis of 3-Acetyl-2-methylpyrrole.*—Aminoacetal (3 g.) with water (1 ml.) was cooled in ice–salt and added dropwise with shaking to hydrochloric acid (18 g.; *d* 1·18). After 5 hr. at room temperature the solution was neutralised to methyl-orange by addition of sodium hydrogen carbonate. Acetylacetone (1·39 g.) was added at once and the pH was brought near to 10 by sodium hydroxide. After 24 hr. at 5° the mixture was saturated with salt and extracted with ether (6 × 15 ml.), which was washed once with saturated salt solution, dried ($MgSO_4$), and evaporated. Sublimation below 100°/0·5 mm. and two crystallisations from light petroleum (b. p. 60—80°) gave white needles, m. p. 94—95° alone or mixed with the product from glucosamine (Found: C, 68·3; H, 7·3; N, 11·7%). The infrared spectra of the two products, in KCl and in $CCl_4$, were identical. No semicarbazone or 2 : 4-dinitrophenylhydrazone could be prepared from 3-acetyl-2-methylpyrrole.

*Preparation of 2-Methylpyrrole.*—Pyrrole-2-aldehyde (5 g.) was added at room temperature to a mixture of potassium hydroxide (10 g.; pellets), 90% hydrazine hydrate (7·5 ml.), and diethylene glycol (100 ml.), from which 2—3 ml. of water had been distilled. After being refluxed for 15 min. the mixture was heated under a take-off condenser so that 2-methylpyrrole (with some water, hydrazine, and glycol) slowly distilled. After 4—5 hr. the condensate was only weakly Ehrlich-positive. To the total distillate (*ca.* 25 ml.) a little water was added; the lower layer was saturated with salt and extracted with ether (4 × 7·5 ml.). The combined upper layers were dried ($MgSO_4$), the ether was removed at −10°/30—40 mm., and the residue was distilled in nitrogen to give 2-methylpyrrole (3·65 g., 86%), b. p. 148°/755 mm. A redistilled sample was analysed (Found: C, 73·9; H, 8·9; N, 17·5%).

From 2-acetylpyrrole (1·5 g.), 2-ethylpyrrole (0·81 g.; b. p. 65°/20 mm.) was similarly obtained.

*Formation of 2-Methylpyrrole at Analytical Concentrations.*—Glucosamine hydrochloride (250 μg.) in water (5 ml.) was mixed with 5 ml. of a solution of acetylacetone (1 ml.) in aqueous 0·5*N*-sodium carbonate (50 ml.). This mixture was heated for 25 min. in a stoppered flask immersed in a bath at 95—100°. After being cooled and shaken the flask was opened and two 1 ml. samples ($O_1$, $O_2$) were withdrawn. The remainder was concentrated at 20 mm. (receiver at −15°). The thawed distillate (slightly under 4 ml.; a pilot experiment had established that this volume contained all the volatile chromogen) was diluted to 8 ml. with water and a 1 ml. portion (D) was taken. The residue (slightly >4 ml.) was also diluted to 8 ml. with water, and two 1 ml. samples ($R_1$, $R_2$) were taken. A solution (P) of 2-methylpyrrole (2·45 μg.) in water (1 ml.) was prepared by suitable dilutions.

Samples $O_1$, D, $R_1$, and P were treated with ethanol (5 ml.) followed, after mixing, by Ehrlich's reagent (0·5 ml. of a solution containing 0·5 g. of *p*-dimethylaminobenzaldehyde in 6 ml. of ethanol and 6 ml. of concentrated hydrochloric acid). Samples $O_2$ and $R_2$ received 0·5 ml. of 1 : 1 ethanol–acid instead of Ehrlich's reagent. A control (B) was prepared from water (1 ml.), ethanol (5 ml.), and Ehrlich's reagent (0·5 ml.). The solutions were left for 1—2 hr. at room temperature for development of colour. Solutions $O_2$ and $R_2$ showed no significant difference from B when examined at 530 or 540 mμ. Solutions $O_1$, D, $R_1$, and P were then measured, with $O_2$ as control. Results are shown in the Table.

| λ | Optical densities | | | | λ | Optical densities | | | |
|---|---|---|---|---|---|---|---|---|---|
| (mμ) | $O_1$ | D | $R_1$ | P | (mμ) | $O_1$ | D | $R_1$ | P |
| 500 | 0·089 | 0·051 | 0·038 | 0·144 | 540 | 0·186 | 0·139 | 0·040 | 0·375 |
| 510 | 0·120 | 0·070 | 0·050 | 0·203 | 544 | — | 0·141 | — | 0·386 |
| 520 | 0·154 | 0·098 | 0·060 | 0·269 | 545 | 0·185 | 0·141 | 0·030 | 0·386 |
| 530 | 0·179 | 0·121 | 0·056 | 0·323 | 550 | 0·176 | 0·138 | 0·025 | 0·377 |
| 535 | 0·183 | 0·132 | 0·050 | — | 560 | 0·125 | 0·100 | 0·020 | 0·287 |

Two solutions (1 ml.) of 3-acetyl-2-methylpyrrole (200 μg. and 10 μg.) in water were treated with ethanol and Ehrlich's reagent as above. After 1 hr. the stronger solution was very pale pink (O.D. 0·05 at 540—560 mμ). After 1 week the stronger solution had become deep purple ($\lambda_{max.}$ 570 mμ); the weaker solution was very pale pink.

*3-Methylbut-3-enal Diethyl Acetal.*—Ethyl orthoformate (90 ml.) and magnesium (35 g.) were stirred and heated at 60°. 2-Methylallyl chloride (*ca.* 2 ml.; freshly distilled) was added, followed by a little methyl iodide. A yellow colour soon appeared; as it faded, an exothermic reaction set in, and cooling was required to keep the temperature below 70°. 2-Methylallyl chloride (49·5 ml.) was then added at a rate which maintained a temperature of 60° (5—6 drops per min.; 4½ hr.) without artificial heating or cooling. Next day the flask was cooled in ice, and saturated aqueous ammonium chloride (*ca.* 40 ml.) was added dropwise until the mixture set solid; the cake was collected on a filter and washed well with ether. The filtrate was evaporated at low pressure and the residue was stirred with water (90 ml.) for 9 hr. The lower layer was saturated with salt and extracted twice with ether. Distillation of the united upper layers gave the *acetal* (IV) (45 g.), b. p. 58—60°/18—19 mm. A redistilled sample, b. p. 56°/17 mm., was analysed (Found: C, 68·6; H, 11·8. $C_9H_{18}O_2$ requires C, 68·3; H, 11·5%); it had b. p. 162°/745 mm., $n_D^{21}$ 1·4155.

*3 : 4-Epoxy-3-methylbutanal Diethyl Acetal.*—The above product (13·2 g.) in ether (20 ml.) was cooled in ice and treated gradually with ethereal M-perphthalic acid (85 ml.), then allowed to warm and kept below 30° by occasional cooling until reaction subsided. Next day phthalic acid was removed by filtration and extraction of the filtrate with aqueous sodium hydrogen carbonate. The dried ($MgSO_4$) solution was distilled to give the *epoxy-acetal* (V) (10·9 g.), b. p. 82—86°/18 mm. A redistilled sample, b. p. 83—84°/17 mm., was analysed (Found: C, 61·8; H, 10·5. $C_9H_{18}O_3$ requires C, 62·0; H, 10·4%).

*4-Amino-3-hydroxy-3-methylbutanal Diethyl Acetal.*—The epoxy-acetal (3 g.) and methanolic ammonia (20 ml.; saturated at 0°) were kept at 37° for 24 hr. Distillation gave the *amino-acetal* (VI) (1·95 g.), b. p. 130°/17 mm. (Found: C, 56·5; H, 10·9; N, 7·2. $C_9H_{21}O_3N$ requires C, 56·6; H, 11·0; N, 7·3%), giving slowly a purple colour with Ehrlich's reagent. Aqueous ammonia, either at 100° for 3½ hr. or at room temperature for 48 hr., also opened the epoxide ring; the best yield of amino-acetal was 65%.

*3-Methylpyrrole.*—The amino-acetal (1·5 g.) was added to a solution of citric acid (4·5 g.) in water (400 ml.), and the solution was distilled, with one interruption to add more water, until the Ehrlich reaction of the distillate became weak. Isolation of 3-methylpyrrole from the distillate (400 ml.) followed the procedure (above) by which 2-methylpyrrole was obtained from glucosamine. The pyrrole (200 mg., 29%) was a clear colourless liquid, b. p. 142—143°/760 mm., which darkened rapidly in air (Found: C, 74·1; H, 8·7; N, 16·5. Calc. for $C_5H_7N$: C, 74·1; H, 8·6; N, 17·3%). A somewhat better yield (38%) was obtained by dissolving the amino-acetal (1 g.) in water (10 ml.) and citric acid (3 g.) and distilling the whole in steam until 400 ml. of distillate had been collected. A mercury complex of the pyrrole was formed when the amino-acetal (250 mg.) was kept with ammonium acetate (450 mg.), 0·5N-acetic acid (2·5 ml.), and mercuric chloride (900 mg.) at 40° for 2 days with occasional shaking.

*General Procedure for Preparing Benzopyrrocolinediones ("Pyrrolene-phthalides").*—The pyrrole (*x* g.) and phthalic anhydride (10*x* g.) were mixed with acetic acid (15*x* ml.) in a tube which was then cooled, constricted, evacuated, sealed, and heated for 2 hr. at 180—190°. The dark brown product was boiled with water, and the black residue was extracted with hot ethanol. The ethanolic filtrate was taken to dryness; the residue was treated with thiophen-free benzene and filtered. The filtrate after concentration was put on a column of alumina (35*x* g.; pretreated with methyl formate and prepared in benzene). On development with benzene a yellow band descended and was collected separately on elution. Evaporation gave the crystalline benzopyrrocolinedione.

3-Methylbenzo[*f*]pyrrocoline-5 : 10-dione [98 mg.; m. p. 171—174° (K)], from 2-methylpyrrole (600 mg.), after two recrystallisations from light petroleum (b. p. 40—60°), formed yellow needles, m. p. 173—174° (K) (Found: C, 73·6; H, 4·3; N, 6·7. Calc. for $C_{13}H_9O_2N$: C, 73·9; H, 4·3; N, 6·6%). Dennstedt and Zimmermann [7] gave m. p. 157° with previous softening. The infrared spectrum (in KCl) was featureless above 1750 cm.$^{-1}$; this was true also of the other benzopyrrocolinediones examined. Bands were observed at 1708 and 1655 cm.$^{-1}$.

A mixture of 1- and 2-methylbenzo[*f*]pyrrocoline-5 : 10-diones (57 mg.) was obtained from 3-methylpyrrole (200 mg.). It was recrystallised from enough ethanol to prevent separation of

the more soluble isomeride; the yellow crystals were washed with light petroleum (b. p. 60—80°) and recrystallised from a little ethanol. 1(or 2)-Methylbenzo[*f*]pyrrocoline-5 : 10-dione formed yellow needles (18 mg.), m. p. 223° (K) (Found: C, 73·9; H, 4·5; N, 6·6. Calc. for $C_{13}H_9O_2N$: C, 73·9; H, 4·3; N, 6·6%). Dennstedt and Zimmermann [7] gave m. p. 215° with previous softening for what is presumably the same product. The mother-liquor and washings from the first recrystallisation were evaporated and the residue was recrystallised from light petroleum (b. p. 40—60°), to give 2(*or* 1)-*methylbenzo*[f]*pyrrocoline*-5 : 10-*dione* (13 mg.) as yellow needles, m. p. 169—170° (K) (Found: C, 73·8; H, 4·5; N, 6·7%). Both isomerides showed ν (in KCl) 1708 and 1655 cm.$^{-1}$.

1-*Ethylbenzo*[f]*pyrrocoline*-5 : 10-*dione* (43 mg.) from 2-ethylpyrrole (364 mg.) formed yellow needles, m. p. 114°, after sublimation *in vacuo* and crystallisation from methanol (Found: C, 74·6; H, 5·0; N, 5·9. $C_{14}H_{11}O_2N$ requires C, 74·7; H, 4·9; N, 6·2%).

1 : 3-*Dimethylbenzo*[f]*pyrrocoline*-5 : 10-*dione*.—(i) The directions of Ingraffia [21] for condensation of 2 : 4-dimethylpyrrylmagnesium bromide (from 6·4 g. of 2 : 4-dimethylpyrrole) and phthalic anhydride (5 g.) in ether were followed. The solid obtained by filtration after decomposition of the mixture with ice and carbon dioxide proved to be soluble in water with a negligible residue and was a magnesium salt of the acid obtained as below. The aqueous filtrate was extracted thrice with ether and acidified. The magnesium salt was dissolved in aqueous ammonium chloride and also acidified. The precipitates were combined (7·2 g.); crystallisation of a portion from methanol (charcoal)–water under nitrogen gave very pale pink crystals, m. p. 195—196·5° (decomp.), of 2-*o*-carboxybenzoyl-3 : 5-dimethylpyrrole (XV; R = Me) (Ingraffia [22] gave m. p. 188°) (Found: C, 68·9; H, 5·2; N, 5·9. Calc. for $C_{14}H_{13}O_3N$: C, 69·1; H, 5·35; N, 5·8%). This acid on being warmed with Ehrlich's reagent developed a cherry-red colour. The acid (100 mg.) was boiled under reflux with water (2 ml.) and ammonia (5 drops; *d* 0·88). After 1·5 hr. the product was collected and recrystallised from a little ethanol, to give 1 : 3-*dimethylbenzo*[f]*pyrrocoline*-5 : 10-*dione* (27·5 mg.), m. p. 181—183° (Found: C, 74·3; H, 4·8; N, 6·4. $C_{14}H_{11}O_2N$ requires C, 74·7; H, 4·9; N, 6·2%), ν (in KCl) 1705, 1650 cm.$^{-1}$; $\lambda_{max.}$ (in EtOH) 378, 318, 267, 237 mμ (log ε 3·67, 3·71, 4·28, 4·42 respectively).

(ii) This dimethylpyrrocolinedione was also obtained on heating 2 : 4-dimethylpyrrole with phthalic anhydride by the standard procedure and was identified by m. p. (181—182·5°), mixed m. p., and infrared spectrum with the sample obtained as above. A specimen (52·5 mg.) was heated with 2N-sodium hydroxide (2 ml.) until dissolution was complete (1 hr.) and the cooled solution was then acidified. The product, crystallised from methanol–water, had m. p. 195—196° (decomp.) alone or mixed with the oxo-acid (XV; R = Me) obtained as above (Found: C, 69·0; H, 5·4; N, 5·9%).

National Institute for Medical Research,
Mill Hill, London, N.W.7.

[*Received, October 29th*, 1957.]

## 218. *The Azulene Series. Part II.* The Synthesis and Properties of Alkoxyazulenes.*

By D. H. Reid, W. H. Stafford, and J. P. Ward.

4- and 5-Methoxyazulene have been synthesised by ring-expansion of the corresponding methoxyindane employing the sequence: reaction with diazoacetic ester, dehydrogenation, hydrolysis, and decarboxylation. The susceptibility of the 4-position to nucleophilic attack is proved by an ether exchange reaction leading to 4-ethoxyazulene. The relation of these substances and their derivatives to alkoxytropylium salts is examined and unsuccessful attempts to prepare 1- and 2-methoxyazulene are recorded. The reactions of azulene with sodamide and other nucleophilic reagents are briefly outlined.

Four claims have been recorded for the preparation of azulene derivatives in which an oxygen atom is directly linked to the seven-membered ring. Analytical purity was not obtained in two instances, 2-ethyl-7-methoxy-4-methylazulene [1] because of a contaminating hydrocarbon, and 4-hydroxyazulene [2] because of inherent instability. Details of the preparation of 4 : 5-dimethoxyazulene [3] are awaited but in the fourth instance, 6-methoxy-1 : 2-benzazulene,[4] the preparation and absorption spectrum have been given. In view of the structural relation [5] of this group of azulene derivatives to the alkoxytropylium salts, routes to the simple alkoxyazulenes were sought.

Treatment of 4-methoxyindane with ethyl diazoacetate, distillation, and hydrolysis of the principal fraction yielded 4-indanyloxyacetic acid [6,7] (I), in 80% yield, together with a crude acid fraction from which no azulenic material could be isolated after dehydrogenation. The balance of the ester fraction, 20%, must contain substantial quantities of ring-expanded material, for direct dehydrogenation of the ester mixture with sulphur gave an overall 8% yield of azulenic products.

Chromatography on alumina resolved the azulenic material into three ethyl methoxyazulenecarboxylates, *A* (blue), *B* (violet), and *C* (blue). *A* and *B* were obtained in a pure crystalline condition and were characterised as their *sym.*-trinitrobenzene complexes. The fraction *C* was present in minute quantities and was isolated conveniently only as its complex. There was no evidence for loss of the methoxyl group at this stage.

Hydrolysis of the ester with ethanolic potassium hydroxide gave an acid which, even after several recrystallisations, did not give satisfactory analyses. The mixed esters *A*, *B*, and *C* were then similarly hydrolysed and the mixed acids immediately treated with quinoline and copper bronze. The decarboxylation product was not homogeneous and chromatography separated a violet compound from azulene. The violet compound, which did not crystallise, was converted into its trinitrobenzene complex which corresponded in analysis to an ethoxyazulene rather than a methoxyazulene. Re-examination of the analytical data for the acid from *A* showed that it too was derived from an ethoxyazulene. It appeared that *A* and probably *B* had suffered displacement of the methoxyl group by an ethoxide ion during the hydrolysis.

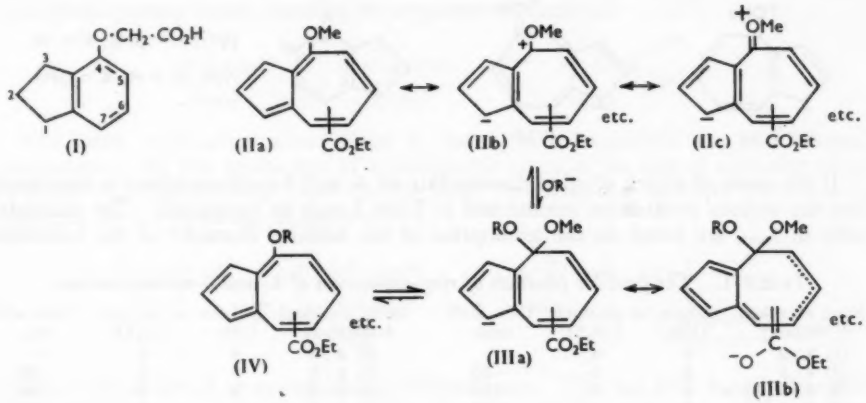
Hydrolysis of the ester mixture with methanolic potassium hydroxide and subsequent decarboxylation gave a new violet compound whose trinitrobenzene complex gave

* Part I, *J.*, 1955, 1193, whose series title, " The Fine Structure of Azulene," has been changed to that given above.

[1] Wagner-Jauregg, Arnold, Hüter, and Schmidt, *Ber.*, 1941, **74**, 1522.
[2] Anderson and Nelson, *J. Amer. Chem. Soc.*, 1951, **73**, 232.
[3] Treibs, *Angew. Chem.*, 1951, **63**, 487.
[4] Treibs and Ziegenbein, *Annalen*, 1955, **595**, 211.
[5] Stafford, Ward, and Reid, *Chem. and Ind.*, 1955, 1258.
[6] Johnson, Bartels-Keith, and Langeman, *J.*, 1952, 4461; Johnson, Langeman, and Murray, *J.*, 1953, 2136.
[7] De Graf, van Dijk-Rothuis, and van de Kolk, *Rec. Trav. chim.*, 1955, **74**, 144.

XUM

satisfactory analyses for a methoxyazulene derivative. The production of azulene was related to the conditions of the decarboxylation; prolonged boiling in quinoline appears to reduce the alkoxyazulene to azulene. A nucleophilic replacement must occur during the alkaline hydrolysis and the resulting expectation that aqueous alkali would produce a hydroxyazulene was realised in practice. It appears likely that esters *A* and *B* are both derived from 4-methoxyazulene and that the ethoxycarbonyl group is necessary to promote the replacement as no corresponding conversion of 4-methoxyazulene into 4-ethoxyazulene could be detected. The annexed general mechanism has been proposed.

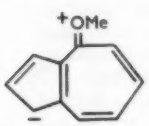



Reaction of 5-methoxyindane with ethyl diazoacetate again gave an ester fraction which on hydrolysis gave a 75% yield of 5-indanyloxyacetic acid. Dehydrogenation of the acidic residues from this gave no azulenic material but the ester fraction suffered smooth dehydrogenation, giving azulenic material in excellent yield. There was no loss of methoxyl during these stages.

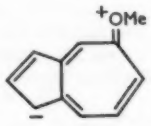
The azulenic fraction was chromatographed and appeared homogeneous although it did not crystallise. It formed a trinitrobenzene complex whose analyses were correct for an ethyl methoxyazulenecarboxylate. The ester was hydrolysed to an acid which was re-esterified with diazomethane. The methyl ester also failed to crystallise and was characterised as its trinitrobenzene complex. Decarboxylation of the acid gave a methoxyazulene which did not solidify but readily formed a trinitrobenzene complex. There was no evidence of ether interchange and during the decarboxylation there was no formation of azulene, indicating higher stability of the 5-C–OMe linkage. It appeared likely that the product was 5-methoxyazulene but the 6-methoxy-structure cannot be eliminated without further evidence. Spectroscopic work points to the former and permits the orientation of the four azulene esters described above.

The visible absorption spectra were in most instances devoid of fine structure and so displacements relative to azulene were measured at the wavelengths of maximum absorption which lie centrally in the visible band. 4-Methoxy- and 4-ethoxy-azulene gave identical curves with a visible maximum at 545 mμ. The corresponding value for azulene is 580 mμ, so that a 4-alkoxy-group causes a hypsochromic displacement of 35 mμ. The colour is consequently violet. The ether derived from 5-methoxyindane showed a bathochromic displacement of 35 mμ to 615 mμ. The possibility of the 6-methoxy-structure can confidently by discounted, for empirically it is known that 4- and 6-substituents of similar character displace the absorption in the same direction, if not always to the same extent. 6-Methoxy-1 : 2-benzazulene is recorded as showing a hypsochromic displacement of 15 mμ relative to the parent hydrocarbon. The Plattner rules indicate that

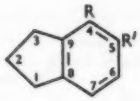
alkyl groups in positions 4 and 5 cause opposite displacements equal in degree—*ca.* 12 mμ. As would be expected, an alkoxy-group shifts absorption in the same direction as an alkyl group but to a greater distance. An electron pair apparently is accepted from the oxygen atom into the molecular orbital, and equivalent polarisations by light absorption require in the 5-case less energy than in the 4-case. If the polarisation is best explained by excited states indicated by such structures as (Va and b), then the energy differences may be associated with the preference of the molecule for a low electron density at the bond of ring fusion (Vb).




(Va)




(Vb)




(VI): R = OMe, R' = H

(VII): R = H, R' = OMe

If the mode of attack of ethyl diazoacetate on 4- and 5-methoxyindane is considered, then the various possibilities summarised in Table 1 may be recognised. The calculated shifts in $\lambda_{max.}$ are based on the assumption of the additive character of the individual

TABLE 1. *The possible products of ring-expansion of 4- and 5-methoxyindane.*

| Bond attacked 4-Methoxy | Substn. in product OMe | Substn. in product $CO_2Et$ | Calc. shift (mμ) | Bond attacked 4-Methoxy | Substn. in product OMe | Substn. in product $CO_2Et$ | Calc. shift (mμ) |
|---|---|---|---|---|---|---|---|
| (1) 4 : 9 | 5 | 4 | * | (6) 4 : 9 | 6 | 4 | * |
| (2) 4 : 5 | 4 | 5 | −50 | (7) 4 : 5 | 6 | 5 | −30 |
| (3) 5 : 6 [A] | 4 | 6 | +20 | (8) 5 : 6 | 5 | 6 | +90 |
| (4) 6 : 7 [B] | 4 | 7 | −50 | (9) 6 : 7 | 5 | 7 | +20 |
| (5) 7 : 8 [C] | 4 | 8 | * | (10) 7 : 8 | 5 | 8 | * |

contributions of the substituent groups. A 5- or 7-ethoxycarbonyl group is assumed [8] to displace it by −15 mμ and a 6-ethoxycarbonyl group by +55 mμ. The values for 4- and 5-methoxy-substituents are those given. That for the 6-methoxy-compound is assumed to be *ca.* −15 mμ.

The shifts found empirically for the esters *A*, *B*, and *C* are +25, −45, and +10 mμ respectively. If possibilities (1) and (5) are ignored then *A* would correspond closely to (3) and *B* to (2) or (4) which cannot be spectroscopically differentiated. This leaves (1) and (5) as possibilities for *C*. Ethyl azulene-4-carboxylate is as yet unknown but it is likely that the shift will be bathochromic, as it is with the 6-ester. As a 5-methoxy-group also gives a large bathochromic shift the small displacement found for *C* appears inconsistent with possibility (1), leaving (5) as the more likely structure. An 8-substituent will be approximately equivalent to a 4-substituent by symmetry, so that a value of +10 mμ can be regarded as the resultant of −35 mμ (4-OMe) and +45 mμ (8-$CO_2Et$). The latter appears a reasonable value. The problem of *B* remains and is discussed in terms of mechanism below.

TABLE 2. *The visible absorption spectra (mμ) of azulene and the ester from 5-methoxyindane.*

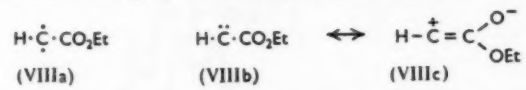
| Peak | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Azulene | 695 | 657 | 627 | 580 | 555 |
| New ester | 705 | 677 | 645 | 612 | 588 |
| Δ | +10 | +20 | +18 | +32 | +33 |

The unique ester from 5-methoxyindane showed fine structure with the characteristic five peaks. In Table 2 they are contrasted with those of azulene. The average displacement is +25 mμ. As the methoxy-group is known to be in the 5-position the ester

[8] Plattner, Fürst, Müller, and Somerville, *Helv. Chim. Acta*, 1951, **34**, 971.

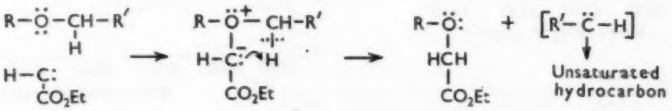
contribution must be −10 mμ. This is consistent with the 5-ester group, leaving only one permissible structure, namely, ethyl 5-methoxyazulene-7-carboxylate.

Thermal decomposition of ethyl diazoacetate is thought to produce a reactive species—ethoxycarbonylmethylene—which is responsible for the various products. There are two possible structures for this intermediate, (VIIIa) and the hybrid (VIIIb and c). The diradical (VIIIa) would attack the substrate in a bidentate manner, separating from a multiple bond or a molecular orbital two electrons to fill the two vacant positions in the partly filled orbitals. With the hybrid structure, attack would involve an electron pair in the substrate and would be essentially electrophilic. A subsequent or concerted nucleophilic process would complete the sequence of reactions.

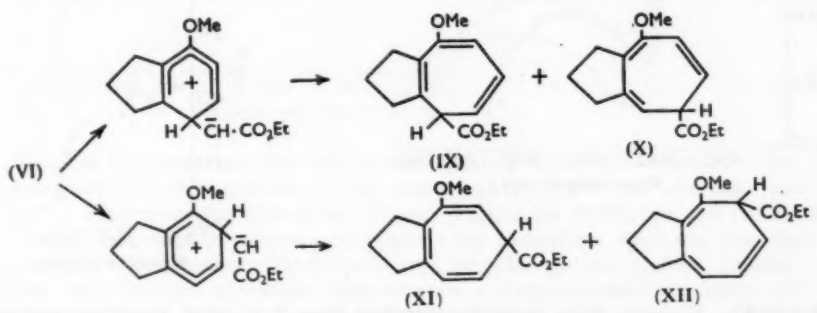


(VIIIa) (VIIIb) (VIIIc)

The latter explanation alone seems to satisfy in a consistent way the following observations. (1) The production of aryloxyacetic esters in the case of aromatic ethers. De Graf, van Dijk-Rothuis, and van de Kolk [7] convincingly interpret this reaction essentially by the following mechanism:




(2) The multiple attack on *cyclo*penta[*def*]phenanthrene. This has been described as more akin to the electrophilic substitution of this system.[9] (3) The production of norcaradiene and *cyclo*heptatriene derivatives singly in related systems. It has been suggested that the latter arise by rearrangement of the initially formed norcaradiene but it appears more likely that rearrangement of some reactive intermediate gives rise to either system. Attack at the 9 : 10-bond in phenanthrene gives a norcaradiene of high stability. *cyclo*-Penta[*def*]phenanthrene suffers analogous attack, but gives the *cyclo*heptatriene derivative.[9] The steric constraint by the five-membered ring must be responsible but it is difficult to attribute such a complete reversal of the stability of a norcaradiene to this alone. (4) Analogous reactive species—the dihalogeno" carbenes "—are, on kinetic evidence, considered to add to olefins by a concerted electrophilic–nucleophilic process.[10]




If this mechanism for the attack on benzenoid compounds is assumed, attack on ethers would occur at the *ortho*- and *para*-positions and the intermediate would pass into the

[9] Reid, Stafford, and Ward, *J.*, 1955, 1193.

[10] Skell and Garner, *J. Amer. Chem. Soc.*, 1956, **78**, 5430; Skell and Woodworth, *ibid.*, p. 4496; Woodworth and Skell, *ibid.*, 1957, **79**, 2542.

product in either or both of two possible ways. With 4-methoxyindane the substances (IX) and (XI) would lead to esters *C* and *A* respectively. Ester *B* could arise from (X) or (XII). If it arose from (XII), the two major products would have arisen from *ortho*-attack. It seems unlikely that there should be only a minor attack in the *para*-position to be represented by *C* alone (in any case the sterically less favoured of products from

FIG. 1. *The product from azulene and sodamide, (A) in* EtOH *and (B) in* 2N-HCl.

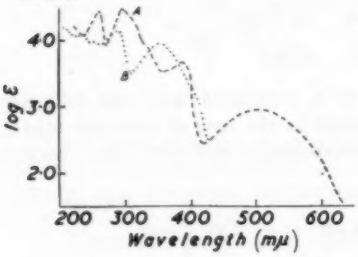



FIG. 2. *(A) Azulene. (B) 4-Methoxyazulene* (log ε + 0·5). *(C) 5-Methoxyazulene* (log ε + 1·0). *All in* EtOH.

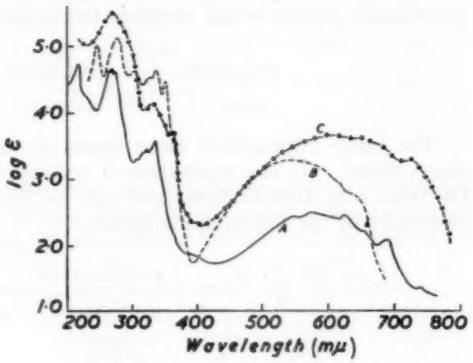



FIG. 3. *Ethyl 4-methoxyazulene-6-carboxylate (A), -7-carboxylate (B), and -8-carboxylate (C); methyl 5-methoxyazulene-5-carboxylate (D). All in* EtOH. (*B and C*, log ε + 0·5.)

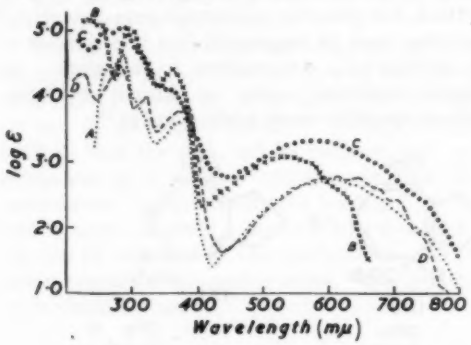
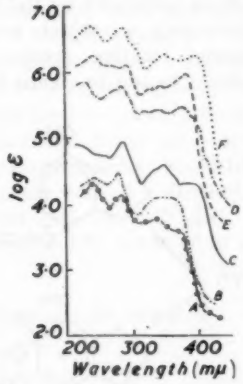



FIG. 4. *4-Ethoxy- (A) and 5-methoxyazulene (B;* log ε + 0·5). *Methyl 5-methoxyazulene-7-carboxylate (C,* log ε + 1·0). *Ethyl 4-methoxyazulene-8-carboxylate (D,* log ε + 1·5), *-7-carboxylate (E,* log ε + 2·0), *and -6-carboxylate (F,* log ε + 2·5). *C and D in* 65% $H_2SO_4$, *the others in conc.* HCl.




*para*-attack). It seems more probable therefore that *B* is ethyl 4-methoxyazulene-7-carboxylate.

5-Methoxyindane could suffer *ortho*-attack at position 4 or 6. Only the latter appears to be involved and sterically this is not surprising. An additional factor may be that the 4-position is activated by an *ortho*-methylene group. whereas the 6-position is activated by a *para*-group. Examples of such preferred electrophilic attack may be found in the

fluorene series, *e.g.*, the 3-position is favoured over the 1-position in substitution of 2-acetamidofluorene.[11]

Synthesis of 1-methoxyazulene [12] by the reaction of ethyl diazoacetate and 1-methoxyindane has been claimed and it is stated that it has a spectrum identical with that of azulene. This appeared surprising. No claim for the preparation of 2-methoxyazulene exists, so samples of 1- and 2-methoxyindane were treated with ethyl diazoacetate. Distillation of both reaction mixtures gave blue oils from which the same single blue substance was isolated by chromatography. The yield of this was increased by taking

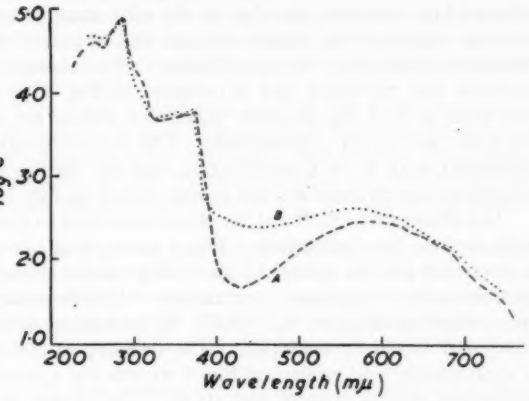



FIG. 5. *4-Hydroxyazulene-6-carboxylic acid* (*A*) *in* EtOH *and* (*B*) *in* 2N-NaOH.

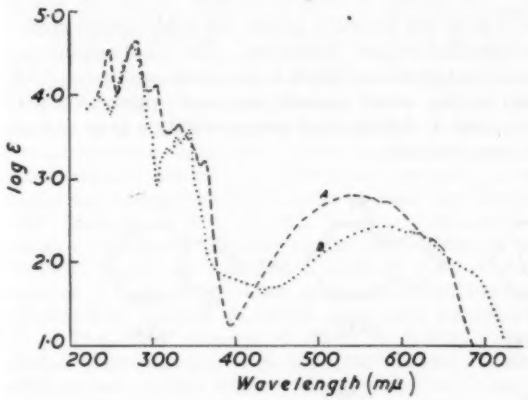



FIG. 6. (*A*) *4-Ethoxyazulene in* EtOH. (*B*) *6-Hydroxymethyleneazulene in* EtOH.

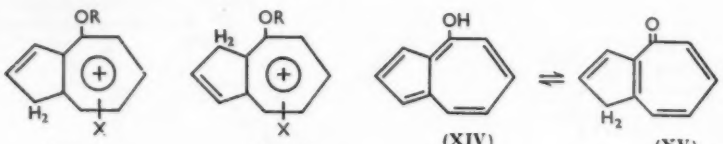
the colourless fractions from the column and treating them with sulphur. This blue compound appeared homogeneous on chromatography. It did not crystallise and did not form a trinitrobenzene derivative. It was purified by distillation and its analyses were correct for an ethyl azulenecarboxylate. Its absorption spectrum was that of ethyl azulene-6-carboxylate. Hydrolysis and decarboxylation yielded azulene and reduction with lithium aluminium hydride gave a hydroxymethyleneazulene with an absorption spectrum consistent with 6-alkyl-substitution. The analysis of the oil is therefore relevant and loss of methanol has occurred during the reaction, presumably after the ring expansion. The resulting dihydroazulene had disproportionated in some way to give the azulene ester.

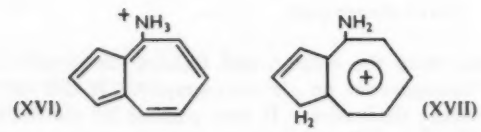
[11] Eckert and Langecker, *J. prakt. Chem.*, 1928, **118**, 263.
[12] Treibs and Stein, *Annalen*, 1951, **572**, 161.

There is accordingly no evidence from our experiments to substantiate the previous surprising claims for the synthesis and properties of 1-methoxyazulene.

One purpose of this work was to provide reference compounds for the orientation of nucleophilic substitution products of azulene. Such compounds have only been available for alkyl-nucleophilic attack and the 4-position has been shown to be involved.[13] Methoxide ion caused degradation of the azulene nucleus, for heating azulene in methanolic potassium methoxide rapidly destroyed the colour. No azulenic compounds were produced by heating the material recovered from these experiments with sulphur. Reaction of azulene with sodamide gave a red unstable basic material: in solution it remained red for some time but in the solid state deterioration was very rapid; a trinitrobenzene complex was readily formed and appeared pure, but analyses of samples from different experiments were inconsistent. The absorption spectrum of the freshly prepared material was measured and is recorded in Fig. 1 (a solution of unknown concentration was used so that the absolute extinction values are unknown; the relative values are, however, accurately represented). The hypsochromic displacement is 75 mμ. This is consistent with 4- or 6-substitution, and the former is likely although not certain. The absorption spectrum of its salt is also shown in Fig. 1.

The absorption spectra of the ethers described in this paper are recorded in Figs. 2 and 3, with azulene for comparison. Fig. 4 gives their absorptions in acid solution. The ions so produced (XIIIa or/and b) have very similar absorptions, consistent with the alkoxy-*cyclo*pentadienotropylium formulation. 4-Hydroxyazulene (XIV) is a tautomer of a *cyclo*pentadienotropone, *e.g.*, (XV); its instability is not due to an equilibrium favouring (XV), but rather to oxidation. The stability of the system is enhanced by the addition of a carboxylic acid group and Fig. 5 records the absorption spectra of 4-hydroxyazulene-6-carboxylic acid in ethanol and alkali. The change in absorption may in part be due to ionisation of the hydroxyl group as well as of the carbonyl group, but acidification always restores the azulene and there is no evidence of tropone formation. The amino-compound in acid is colourless. It is to be expected that proton addition to the amino-group (cf. XVI) would give a blue or violet compound as this would remove electronic interaction with the azulene moiety. As this does not occur, it follows that proton addition is to carbon, giving an aminotropylium compound, *e.g.*, (XVII).




The general picture for these absorption spectra conforms to the findings of Plattner and his co-workers [14] for the alkylazulenes and their ester derivatives, and of Heilbronner and his associates [15] for the alkoxytropylium and tropylium derivatives. The absorption spectra of 6-hydroxymethylene- and 4-ethoxy-azulene are given in Fig. 6.

[13] Hafner and Weldes, *Angew. Chem.*, 1955, **67**, 302.
[14] Plattner and Pfau, *Helv. Chim. Acta*, 1937, **20**, 224; Plattner, Fürst, and Schmid, *ibid.*, 1945, **28**, 1647.
[15] Rennhard, di Modica, Simon, Heilbronner, and Eschenmoser, *ibid.*, 1957, **40**, 961.

XUM

## Experimental

Ligroin refers to the fraction of b. p. 40—60°.

*Thermal Decomposition of Ethyl Diazoacetate in Alkoxyindanes.—General method.* The alkoxyindane (30—40 g.) was heated at 140°, with stirring, under an air-condenser drawn to a capillary. Ethyl diazoacetate (10—15 g.) was added dropwise during 3 hr. The mixture was then heated at 200° for a further 2 hr. and distilled under reduced pressure.

*Isomeric Ethyl 4-Methoxyazulenecarboxylates.*—4-Methoxyindane (30·0 g.; b. p. 127—128°/31 mm.) was treated with ethyl diazoacetate (13 g.). Distillation yielded fractions, (i) a colourless liquid (3·0 g.; b. p. 72—75°/47 mm.), (ii) unchanged 4-methoxyindane (17·0 g., b. p. 133°/50 mm.), (iii) unchanged 4-methoxyindane (2·0 g., b. p. 85°/1·5 mm.), (iv) a mobile oil, green in reflected light, red in transmitted light (4·5 g., b. p. up to 150°/0·3 mm.), and (v) a viscous red oil (2·4 g., b. p. 180°/0·3 mm.). A residual brown tar accounted for the balance. Fractions (ii) and (iii) were combined and recycled.

The fraction (iv) from two cycles (7·0 g.) was heated with sulphur (2·0 g.) for 5 min. in a preheated oil-bath at 200°. The colour changed to dark blue-green and hydrogen sulphide was evolved. No advantage is served in prolonging the reaction. The mixture was cooled, dissolved in the minimum quantity of benzene, and chromatographed on neutral alumina, yielding (i) a broad blue band eluted with benzene–ligroin (1 : 1) and (ii) a green band eluted with benzene.

The blue eluate was diluted with ligroin (250 ml.) and extracted with successive portions (50 ml.) of cold syrupy phosphoric acid until no further orange colour appeared in the acid layer. Sulphur and a little green material were retained in the organic layer. The combined acid layers were washed with 1 : 1 benzene–ligroin (250 ml.) and poured into ice-water. An ether extract of the resulting blue precipitate, dried ($Na_2SO_4$) and evaporated, yielded a mobile blue oil (510 mg.).

The green eluate gave an oil (2·1 g.), which contained a little sulphur, yielded 4-indanyloxyacetic acid on hydrolysis, and gave no more blue material on further dehydrogenation.

Dehydrogenation of a further quantity of fraction (iv) by 20% palladium–charcoal for 8 min. at 240° gave a blue oil (130 mg.) (recovered from phosphoric acid) and a green oil (0·7 g.). Dehydrogenation of fraction (v) (2 g.) with sulphur gave a small amount of the blue oil (30 mg.).

The combined blue oils (650 mg.) were chromatographed, giving the following products: (A) On elution with benzene–ligroin (1 : 9), a blue oil (380 mg.) which yielded a crystalline *s*-trinitrobenzene derivative. This was recrystallised until pure and was then decomposed on an alumina column with elution by the same solvent mixture. *Ethyl 4-methoxyazulene-6-carboxylate* crystallised from ligroin as dark blue blades with a green reflection, m. p. 63·5—64·5° (Found: C, 73·1; H, 6·2. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1%). The *trinitrobenzene complex* crystallised as brown needles (from ethanol), m. p. 90—92° (Found: C, 53·7; H, 3·7; N, 10·0. $C_{19}H_{17}O_9N_3$ requires C, 54·2; H, 3·9; N, 9·5%). (B) On elution with 1 : 1 ligroin–benzene, a violet eluate which gave a violet oil (200 mg.). This was rechromatographed until an ethanolic solution deposited pure *ethyl 4-methoxyazulene-7-carboxylate* as violet needles, m. p. 76·5—77·5° (Found: C, 73·2; H, 6·1%). The *trinitrobenzene complex* formed orange needles (from ethanol), m. p. 102—103° (Found: C, 53·7; H, 3·6; N, 9·4%). (C) On elution with benzene, a blue eluate yielding a blue oil (8 mg.). *Ethyl 4-methoxyazulene-8-carboxylate* formed a trinitrobenzene complex, brown plates, m. p. 123° (Found: C, 54·1; H, 4·0; N, 9·2%).

*4-Ethoxyazulene-6-carboxylic Acid.*—Ethyl 4-methoxyazulene-6-carboxylate (125 mg.) was boiled in ethanol (25 ml.) containing potassium hydroxide (1·0 g.) for 2 hr., then diluted with water (150 ml.). The neutral material was separated by ether-extraction, and the acidic product recovered from the violet aqueous layer by acidification and further extraction. The blue extract yielded a green solid (100 mg.). *4-Ethoxyazulene-6-carboxylic acid* crystallised from benzene–ethanol as green needles, m. p. 234—236° (decomp.) (Found: C, 72·1; H, 5·4. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6. $C_{12}H_{10}O_3$ requires C, 71·3; H, 5·0%).

*4-Hydroxyazulene-6-carboxylic Acid.*—Ethyl 4-methoxyazulene-6-carboxylate (30 mg.) was treated as above, but with aqueous potassium hydroxide, and yielded *4-hydroxyazulene-6-carboxylic acid* (20 mg.), green needles (from benzene–ethanol), m. p. 236° (decomp.) (admixture with the previous acid gave a depression to 195—230°) (Found: C, 69·6; H, 4·8. $C_{11}H_8O_3$ requires C, 70·2; H, 4·3%).

*4-Ethoxyazulene.*—Unseparated isomeric esters (190 mg.) were hydrolysed with ethanolic

potassium hydroxide as above, to give acids (140 mg.), which were heated with copper bronze (1 g.) in quinoline (20 ml.) at 240° for 45 min., then dissolved in ether. The decarboxylation product was freed from quinoline by extraction with dilute hydrochloric acid and from unchanged acids by extraction with sodium hydrogen carbonate solution. The neutral material was chromatographed on alumina, to give: (i) On elution with ligroin, a blue oil (4 mg.) which showed some tendency to crystallise. It was converted into a trinitrobenzene complex, m. p. 166—167°, identical with that of azulene. (ii) On elution with benzene–ligroin (1 : 3), a violet oil (12 mg.); this ether formed a *trinitrobenzene derivative*, red-brown needles, m. p. 143°, from ethanol (Found: C, 56·2; H, 4·0; N, 10·4. $C_{19}H_{15}O_7N_3$ requires C, 56·1; H, 3·9; N, 10·9%). The ether was volatile in organic solvents.

*4-Methoxyazulene.*—Mixed esters (110 mg.) were converted by methanolic potassium hydroxide into acids (80 mg.) which were decarboxylated as above. Chromatography gave a trace of azulene and a violet oil (7 mg.) which was converted into its *trinitrobenzene derivative*, red-brown needles (from ethanol), m. p. 163° (Found: C, 55·2; H, 3·6; N, 10·8. $C_{17}H_{13}O_7N_3$ requires C, 55·0; H, 3·5; N, 11·3%). 4-Methoxyazulene co-distils with organic solvents. Reducing the time of the decarboxylation by one half gave a better yield (90 mg. of acid gave 14 mg. of ether) and no azulene. Further reduction of the time led to a lower yield and recovery of most of the starting acid.

*4-Indanyloxyacetic Acid.*—Fraction (iv) (720 mg.) with ethanolic potassium hydroxide (3%) for 2 hr. gave an acid (600 mg.) which formed prisms, m. p. 184° (480 mg.), from benzene. This was identical (mixed m. p.) with *4-indanyloxyacetic acid* prepared from 4-hydroxyindane in the normal manner (Found: C, 68·6; H, 6·4. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%). The benzene mother-liquors contained a green acidic oil. Similarly, fraction (v) gave a small portion of the phenoxyacetic acid and a quantity of the oil. The combined oils gave no azulenic materials on dehydrogenation.

*Ethyl 5-Methoxyazulene-7-carboxylate.*—5-Methoxyindane (40 g.) (prepared from the phenol and dimethyl sulphate in the normal manner; b. p. 143—145°/60 mm.) was treated with ethyl diazoacetate in the usual way. Distillation yielded fractions: Unchanged 5-methoxyindane (i) 25·5 g., b. p. 132°/39 mm.; (ii) 1·9 g., b. p. 95°/0·6 mm.; (iii) a mobile green oil (6·8 g.), b. p. up to 145°/0·6 mm.; (iv) a viscous green oil (2·3 g.), boiling up to 190°/0·6 mm. There was a residual tar (12·5 g.). Fractions (i) and (ii) were recycled.

Fraction (iii) (8·0 g.) was heated with sulphur (2·0 g.) in a preheated oil-bath at 200° for 5 min. The mixture was cooled, taken into benzene, and chromatographed on alumina. Elution with benzene–ligroin (1 : 3) gave a blue eluate, and with benzene a green eluate. The blue eluate was diluted with ligroin and extracted with phosphoric acid. The acid extract was washed with ligroin and diluted with water. An ether-extract of the resulting blue precipitate was dried ($Na_2SO_4$) and gave a blue oil (710 mg.) which was rechromatographed. No separation into fractions was achieved and only one blue band was eluted. *Ethyl 5-methoxyazulene-carboxylate* did not crystallise even when recovered from its *trinitrobenzene derivative*, brown needles (from ethanol), m. p. 70° (Found: C, 53·9; H, 3·8; N, 9·7. $C_{20}H_{17}O_9N_3$ requires C, 54·2; H, 3·9; N, 9·5%). This ester was hydrolysed to the acid by ethanolic potassium hydroxide; the acid was treated with diazomethane but the methyl ester thus obtained did not crystallise. It (methyl 5-methoxyazulene-7-carboxylate) gave a *trinitrobenzene complex*, brown needles (from ethanol), m. p. 118° (Found: C, 53·3; H, 3·7; N, 9·8. $C_{19}H_{15}O_9N_3$ requires C, 53·2; H, 3·5; N, 9·8%).

*5-Methoxyazulene.*—Ethyl 5-methoxyazulene-7-carboxylate (180 mg.) was hydrolysed with ethanolic potassium hydroxide to an acid (140 mg.). This was decarboxylated as usual and chromatography of the neutral material, freed from quinoline and unchanged acid, gave on elution with benzene–ligroin a single blue band, yielding a blue oil (18 mg.). This oil did not crystallise but gave a *trinitrobenzene derivative*, black needles (from ethanol), m. p. 125° (Found: C, 55·0; H, 3·4; N, 11·3. $C_{17}H_{13}O_7N_3$ requires C, 55·0; H, 3·5; N, 11·3%). 5-Methoxyazulene was volatile in organic solvents.

*5-Indanyloxyacetic Acid.*—A portion of fraction (iii) (1·0 g.) was hydrolysed with boiling 3% ethanolic potassium hydroxide (30 ml.) for 2 hr. The acidic product was a green oil (0·8 g.) which deposited colourless plates (580 mg.), m. p. 157°, from benzene (Found: C, 68·7; H, 6·6. Calc. for $C_{11}H_{12}O_3$: C, 68·7; H, 6·3%). Kruber gives m. p. 157°. No depression was observed in a mixed m. p. with a sample made by his method.

*Reaction of 2-Methoxyindane with Ethyl Diazoacetate.*—2-Hydroxyindane (42 g.) with methyl

iodide and silver oxide gave 2-*methoxyindane* (32 g.), b. p. 100—103°/14—15 mm. (Found: C, 81·0; H, 8·1. $C_{10}H_{12}O$ requires C, 81·0; H, 8·2%). This (32 g.), treated with ethyl diazoacetate (12·0 g.) and distilled, yielded: Unchanged 2-methoxyindane (i) (27·2 g.), b. p. 98—100°/12 mm., (ii) (1·8 g.), b. p. 70°/0·3 mm., (iii) a deep blue oil (6·2 g.), b. p. 180°/0·3 mm., and (iv) a viscous green oil (1·5 g.), b. p. 180—200°/0·3 mm.

Fraction (iii) (3·3 g.) was chromatographed on alumina, to give fractions: (A) On elution with benzene–ligroin (1 : 3) a blue oil (1·8 g.). (B) On elution with ethanol a green oil (1·5 g.). The latter was heated with sulphur (0·5 g.) for 5 min. at 200° and the product chromatographed on alumina, to give a further quantity (160 mg.) of the blue oil. The combined blue oils were taken into ligroin and extracted with phosphoric acid. The acid extract was diluted and the blue precipitate was taken into ether and dried ($Na_2SO_4$). The blue oil obtained from this extract was chromatographed. Only a single band was obtained and it appeared to be homogeneous. The compound was distilled in a short-path still (bath 120°/$10^{-5}$ mm.) (Found: C, 77·8; H, 6·7. Calc. for $C_{13}H_{12}O_2$: C, 78·0; H, 6·1%). It appeared to be ethyl azulene-6-carboxylate which is known. It did not form a trinitrobenzene complex.

The blue oil (1·0 g.) was hydrolysed with 3% ethanolic potassium hydroxide and the resulting acid was decarboxylated in quinoline with copper bronze. Chromatography of the neutral product gave a single blue-violet eluate which gave a crystalline residue of azulene (85 mg.). The trinitrobenzene derivative of this had m. p. and mixed m. p. 166—167°.

6-*Hydroxymethylazulene*.—The blue oil (300 mg.) was reduced with lithium aluminium hydride (60 mg.) in dry ether (50 ml.). The deep blue colour of the ester was replaced within a few minutes by the less intense colour of the reduction complex. On the addition of water the blue colour reappeared. The product was chromatographed on alumina, giving several bands: (i) On elution with combinations of ligroin–benzene–ether faint pink, blue, and green bands which contained insignificant quantities of material. (ii) On elution with 1 : 9 ethanol–ligroin a blue substance (190 mg.) which crystallised from benzene as violet-blue plates, m. p. 116—118°. The *alcohol* (Found: C, 83·3; H, 6·8. $C_{11}H_{10}O$ requires C, 83·5; H, 6·4%) failed to give a trinitrobenzene complex.

The use of 1-methoxyindane gave the same results as that of 2-methoxyindane.

4-*Aminoazulene*.—Sodamide was formed in liquid ammonia (200 ml.) from sodium (2·0 g.) and ferric nitrate (0·1 g.). When the blue colour was completely dispelled, azulene (240 mg.) in ether (10 ml.) was added. The mixture was agitated several times during 5 hr. Excess of ammonia was expelled and moist ether was added to decompose the complex. Ethanol and finally water were employed to decompose the sodamide. The violet ether layer was separated, washed with water, and extracted with 4N-hydrochloric acid. Azulene (40 mg.) was retained in the ether, and addition of sodium hydroxide to the acid layer precipitated red material. This was taken into ether and after this extract had been dried ($Na_2SO_4$) the ether was removed, leaving a bright red crystalline residue (120 mg.). Within a few minutes a brown crust had been formed which was insoluble in warm ethanol. Solutions of this red compound appeared stable, and from ethanol a crystalline trinitrobenzene derivative was isolated as brown needles, m. p. 218° (decomp.). Analyses of this derivative from several preparations proved unsatisfactory. The carbon–hydrogen values were reasonable but the nitrogen value was very low and variable, probably owing to oxidation or hydrolysis (Found on 2 samples: C, 54·4, 53·9; H, 3·6, 3·4; N, 13·9, 12·9. Calc. for $C_{16}H_{12}O_6N_4$: C, 53·9: H, 3·4; N, 15·7%).

We thank the British Petroleum Co. Ltd. for a grant.

THE CHEMISTRY DEPARTMENT,
THE UNIVERSITY, EDINBURGH, 9.

[*Received, August 12th*, 1957.

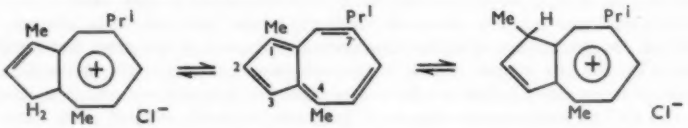
o o

## 219. *The Azulene Series. Part III.* The Synthesis and Properties of 3-Benzylideneguaiazulenium Chloride.*

By D. H. Reid, W. H. Stafford, Winifred L. Stafford, and (in part) G. McLennan and A. Voigt.

The synthesis of 3-benzylideneguaiazulenium salts is recorded and their reactions with nucleophilic reagents are discussed.

While studying the Gattermann reaction,[1] it was observed that a solution of guaiazulene (1 : 4-dimethyl-7-*iso*propylazulene) (I) in methylene chloride became colourless when saturated with hydrogen chloride. The conversion into guaiazulenium chloride (IIa and/or b) must then be complete. The methylene group in (IIa) would be expected to be reactive, by analogy with indene and 1 : 2-dialkylpyridinium salts.[2] Indeed, addition of benzaldehyde caused the rapid deposition of orange crystals. Many aromatic aldehydes readily caused this reaction but aliphatic aldehydes and ketones either did not react or gave products of a different type.




(IIa) (I) (IIb)

When ether was used as a solvent the blue colour remained at saturation but addition of the aldehyde still produced the orange precipitate. An equilibrium must exist here between (I) and (IIa and/or b), reaction with an excess of aldehyde causing eventual consumption of all the azulene. This proved to be the more convenient preparative procedure as the methylene chloride required purification on each occasion before use.

The orange substance formed by benzaldehyde was unstable. In a few hours its solubility had altered markedly and the solid had become brown, especially on the surface. It was extremely insoluble in non-hydroxylic solvents and rapidly changed to a blue material in hydroxylic solvents. Only in glacial acetic acid, and similar acids, was it reasonably stable. Analysis proved difficult owing to the instability and to failure to effect recrystallisation. In the freshly prepared material the chloride ion content was slightly high owing to apparent occlusion of hydrogen chloride. However, addition of saturated aqueous picric acid to an acetic acid solution of the chloride caused crystallisation of a picrate: this was stable for a few weeks but could not be crystallised as it was degraded by hot solvents. The crude material gave satisfactory analyses and the method was generally applicable, except to *m*-bromobenzaldehyde (here formic acid had to be used to prevent the decomposition). The analytical values showed that reaction was between one molecule each of azulene and aldehyde, giving a fulvene derivative, 3-benzylideneguaiazulenium chloride (III), or occurring at the 4-methyl group (IV).

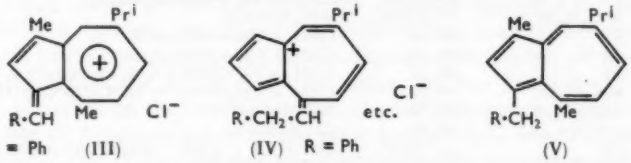
Reduction of the blue *pseudo*-base derived from the salt by treatment with alkali gave no useful result because of complexity of the reaction with bases. Direct reduction of the salt, catalytically or with lithium aluminium hydride, gave a blue hydrocarbon. This did not crystallise or give a crystalline trinitrobenzene derivative: all the liquid hydrocarbons reported in this paper decomposed owing to oxidation, whereas related crystalline compounds were reasonably stable, presumably because of more rapid diffusion of oxygen through the liquid.

* Part II, preceding paper.

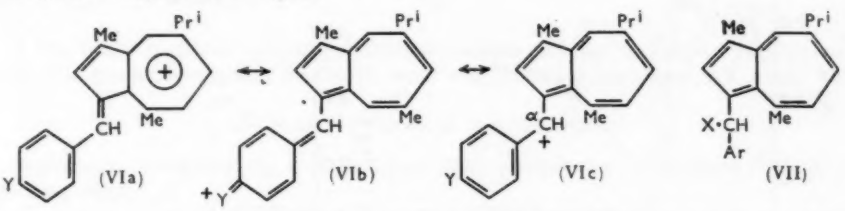
[1] Part IV, following paper.

[2] Reid and Stafford, *Chem. and Ind.*, 1954, 277.

The liquid hydrocarbon showed an absorption maximum in the visible region at 630 mμ which is +25 mμ displaced from the position for the parent guaiazulene, in agreement with a new 3-alkyl substituent, as in (V). The alternative, derived from (IV), should




have an absorption identical with that of guaiazulene. It therefore appeared likely (but not certain) that structure (III) was correct for the salt. *m*-Bromobenzaldehyde gave a salt which on reduction with lithium aluminium hydride yielded a crystalline compound giving correct analyses for 3-*m*-bromobenzylguaiazulene (V; R = *m*-Br·C$_6$H$_4$) and having an absorption spectrum identical with that of the liquid presumed to be 3-benzylguaiazulene (Fig. 1). The molecular weight, determined by *X*-ray crystallography, confirmed its monomeric character. The bromo-compound did not form a trinitrobenzene derivative: of the several 3-alkylguaiazulenes prepared none has given a complex: this may be due to steric interaction between the 3-benzyl substituent and the 4-methyl group which forces the phenyl group out of planarity with the azulene moiety, thus preventing the required packing in the crystalline complex.




These salts are formally fulvene derivatives, and the absorption spectra of derivatives from benzaldehydes possessing electron-donating substituents showed the expected shifts (Table 1). This is explained by enhanced contribution of forms analogous to (VIb),

TABLE 1. *The visible absorption maxima of substituted* 3-*benzylideneguaiazulenium salts.*

| Guaiazulenium cation | $\lambda_{max.}$ (mμ) |
|---|---|
| 3-Benzylidene | 452 |
| 3-3′-Bromobenzylidene | 452 |
| 3-2′-Methoxybenzylidene | 496 |
| 3-4′-Methoxybenzylidene | 518 |
| 3-Piperonylidene | 530 |
| 3-*p*-Dimethylaminobenzylidene (in NaOAc–AcOH) | 640 |

extending the molecular orbital by the assumption of an electron pair from the group Y. In agreement with this is the degree to which *o*-methoxy-, *p*-methoxy-, methylenedioxy-, and *p*-dimethylamino-groups affect the absorption and also the cancellation effect of the last group in concentrated hydrochloric acid.

Salts such as (VI) should be liable to nucleophilic attack, at the α-carbon atom (cf. VIc) or at a free position in the 7-membered ring, or an alkyl group (*e.g.*, 4-methyl) might lose a proton. As the first possibility was the most likely, attack by hydroxide ion was regarded initially as giving the substance (VII; X = OH); it was assumed that the yellow colour obtained by dissolving the "*pseudo*-base" in acid was due to reversion to the salt (III). It was later shown that most of the complex hydrocarbons described below gave similar colours in acid and that the "*pseudo*-base" was an intractable and constantly changing mixture. A series of nucleophilic reagents was investigated and an extemely complex

TABLE 2. *The action of nucleophilic reagents on 3-arylideneguaiazulenium salts.*

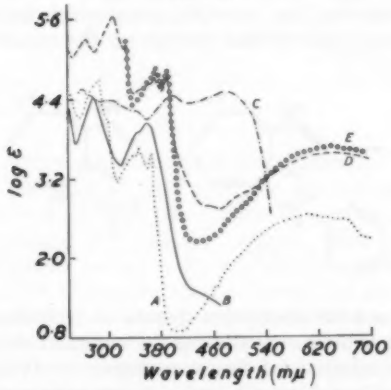
| No. | Ar in Ar·CH= | Reagent | Products [a] |
|---|---|---|---|
| 1 | Ar [c] | MeMgI | Ar·CHMe·Gu |
| 2 | Ph | PhMgBr | $CH_2Ph·Gu_2$ (hydrocarbon A) |
| 3 | *m*-$C_6H_4Br$ | PhMgBr | Ar·CHPh·Gu |
| 4 | Ph | KOEt | GuH + hydrocarbon B |
| 5 | Ar [b] | KOEt | GuH + $CH_2Ar·Gu_2$ |
| 6 | Ph | KCN | GuH + NC·CHPh·Gu + hydrocarbon C |
| 7 | *m*-$C_6H_4Br$ | KCN | GuH + $CH_2Ar·Gu$ + NC·CHAr·Gu·CHGu(CN) |
| 8 | *o*-MeO·$C_6H_4$ | KCN | NC·CHAr·Gu |
| 9 | *p*-$NO_2·C_6H_4$ | KCN | $CH_2Ar(Gu)_2$ |
| 10 | Ph | Ar·$NH_2$ [c] | Ar·$NH_2Cl$ + GuH + hydrocarbon D |
| 11 | *m*-$C_6H_4Br$ | Ph·$NH_2$ | GuH + $(CH_2Ar)_2(Gu)_7$ |

[a] Gu = guaiazulene residue. [b] Ar = Ph, 3 : 4-$(MeO)_2C_6H_3$, *p*-MeO·$C_6H_4$, or *m*-$C_6H_4Br$. [c] Ar = *m*-$C_6H_4Br$, 3 : 4-$(MeO)_2C_6H_4$, or *p*-MeO·$C_6H_4$. [d] Ar = Ph or *p*-$C_6H_4Cl$.

picture, summarised in Table 2, emerged. It is remarkable, however, that, in spite of this complexity, each experiment was reproducible and gave only a few products.

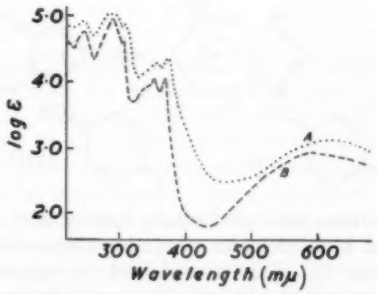
The products from the reaction with methylmagnesium iodide were all liquids of the expected composition and visible absorption ($\lambda_{max.}$ 630 mμ). Phenylmagnesium bromide

FIG. 1.




*(A) Guaiazulene (in hexane). (B) Guaiazulenium chloride (in methylene dichloride). (C) 3-Benzylideneguaiazulenium chloride (in* 10N-HCl). *(D) 3-Benzylguaiazulene (in hexane)* (log ε + 1·0). *(E) 3-3′-Bromobenzylguaiazulene (in hexane)* (log ε + 1·0).

FIG. 2.




*(A) Hydrocarbon and (B) dinitrile from the reaction of 3-3′-bromobenzylideneguaiazulenium chloride and potassium cyanide.*

with the benzylidene salt gave a crystalline product, unexpectedly composed of two guaiazulene residues per benzylidene residue (as shown by the *X*-ray molecular weight). The bromobenzylidene salt on the other hand gave a substance giving approximately the correct analysis for 3-(*m*-bromo-α-phenylbenzyl)guaiazulene, though perhaps containing a little of the diguaiazulene compound analogous to that mentioned above.

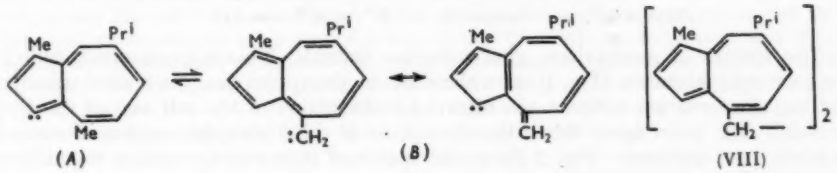
With potassium ethoxide several arylidene salts gave guaiazulene and a substance containing two guaiazulene residues for each arylidene residue. If a hydrocarbon B from the benzylidene salt conforms with the others it is an isomer of hydrocarbon A.

With potassium cyanide the benzylidene salt gave guaiazulene, a hydrocarbon C, and a nitrile, aqueous conditions favouring production of nitriles and anhydrous media that of hydrocarbons. The nitrogenous product from the benzylidene salt was the expected α-cyanobenzylguaiazulene, as shown by its analysis, *X*-ray molecular weight, and oxidation on treatment with alkali to 3-benzoylguaiazulene (cf. following paper). The hydrocarbon C did not yield a single crystal of sufficient size for an *X*-ray molecular-weight determination.

The nitrile from the bromobenzylidene salt was derived from two guaiazulene and one bromobenzylidene residue and contained two cyanide groups. Treatment with alkali again effected oxidation, to a diketone, whose absorption spectrum suggested that the dicyanide was that shown in the Table and the diketone $Br{\cdot}C_6H_4{\cdot}CO{\cdot}Gu{\cdot}CO{\cdot}Gu$; the position of linking is however uncertain. The hydrocarbon contained three guaiazulene residues for each bromobenzylidene residue, showing the critical effect of small differences in molecular structure of the arylidene salt (cf. nos. 8 and 9 in Table 2).

The action of aniline on the benzylidene salt gave a hydrocarbon D containing a little nitrogen, but use of *p*-chloraniline gave the same hydrocarbon free from nitrogen and chlorine; this substance crystallised as minute needles and it proved impossible to obtain a single crystal for a molecular-weight determination. The corresponding substance from the bromobenzylidene salt had an analysis consistent with seven guaiazulene residues for two benzylidene residues.

It is apparent that in a few instances the expected nucleophilic attack at the α-carbon atom has occurred, yielding substances of the general form (VII).



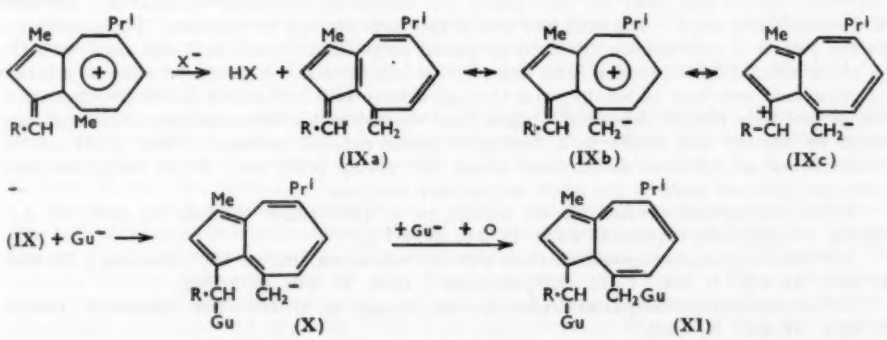

A hydrocarbon containing two guaiazulene residues and one benzylidene residue could result if a guaiazulene anion results in some way from the arylidene salt under basic attack:

$$Ar{\cdot}CH{:}Gu^+ + Gu^- \longrightarrow Ar{\cdot}CH{\cdot}Gu{\cdot}Gu$$

The anion may be derived by a displacement from a substance of structure (VII) by an attacking anion:

$$Ar{\cdot}CHX{\cdot}Gu + Y^- \longrightarrow Ar{\cdot}CHXY + Gu^-$$

The guaiazulene anion, by abstracting a proton from some source, would give guaiazulene, which is a product in most reactions; otherwise it could participate in the formation of a diguaiazulenylphenylmethane. Two such isomeric substances have been obtained, so two types of azulene anion may exist, *e.g.*, *A* and *B*. The form *A* would be stabilised as its magnesium derivative in the Grignard reaction, but form *B* is otherwise probably more stable.

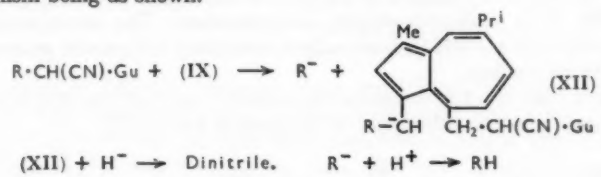



Now guaiazulene, when treated with sodamide, suffers oxidation to a dimer whose absorption spectrum is identical with that of the monomer. It appears that an anion

formed by nucleophilic attack is oxidised, which might cause linking of two alkyl side-chains, as in (VIII). The oxidative linking of a complex anion with a guaiazulene anion, as in the annexed scheme, yields substances containing larger proportions of guaiazulene residues.

The initial abstraction of a hydrogen atom accounts for appearance of aniline as its hydrochloride, a mode of attack which is analogous to reaction of substances such as α-picoline methiodide.

The dicyanide from the bromobenzylidene salt would result if an anion attacking the cyanide (VII; X = CN) displaced a bromophenyl instead of a guaiazulene anion, the overall mechanism being as shown.




The spectra of guaiazulene, guaiazulenium chloride, 3-benzylguaiazulene, and 3-*m*-bromobenzylguaiazulene (Fig. 1) show the shifts in absorption due to a 3-alkyl substituent and the close relation between the ultraviolet absorption of the salt and of the hydrocarbons. The same figure shows the absorption of the 3-benzylideneguaiazulenium salt which is quite different. Fig. 2 shows the spectrum of one of the nitriles together with that of the accompanying hydrocarbon, to demonstrate that the cyano-group modifies the contribution of the 3-alkyl substituent.

## Experimental

The procedure for chromatography was the following. An ether extract of the products was washed with water, dried ($Na_2SO_4$), and evaporated. The residue was dissolved in light petroleum (b. p. 40—60°) containing, where necessary, a little benzene, and chromatographed on alumina. The solvents used for elution were (i) light petroleum (b. p. 40—60°)–ether, (ii) mixtures of this with increasing proportions of benzene, (iii) benzene, (iv) benzene–ether, (v) ether, (vi) ether–ethanol, and (vii) ethanol. Densities of crystals were determined by the flotation method, with aqueous potassium mercuri-iodide to which it was necessary in many instances to add ethanol to " wet " the crystals.

*Condensation of Guaiazulene with Aromatic Aldehydes.—General methods.* Dry ether (50 ml.) was saturated with hydrogen chloride. Guaiazulene (1 g.) and the aldehyde (*ca.* 1·5 mols.) were added while the flow of hydrogen chloride was continued. A microcrystalline solid was deposited rapidly and, after the blue colour was completely dispelled, the solid was collected and washed with ether. The solid was used in this form directly for reaction. For preparation of the picrate it was usually dissolved in glacial acetic acid (formic acid was used with the *m*-bromobenzaldehyde product), and this solution was filtered. A saturated aqueous solution of picric acid was then added dropwise through a filter with continuous shaking. Crystals of the picrate were rapidly deposited. These were washed with a little aqueous acetic acid, and dried by suction and finally in a desiccator under reduced pressure. They could not be recrystallised as solutions decomposed above 50°, giving green tar. These crude materials were analysed and gave on the whole satisfactory analyses:

3-*Benzylideneguaiazulenium picrate*, orange, m. p. 101—102·5° (Found: C, 65·7; H, 5·1; N, 8·1. $C_{28}H_{25}O_7N_3$ requires C, 65·2; H, 5·0; N, 8·1%).

3-4′-*Methoxybenzylideneguaiazulenium picrate*, red-brown, m. p. 150° (decomp.) (Found: C, 64·7; H, 5·2; N, 8·4. $C_{29}H_{27}O_8N_3$ requires C, 63·8; H, 5·0; N, 7·7%).

3-2′-*Methoxybenzylideneguaiazulenium picrate*, orange, m. p. 103—106° (decomp.) (Found: C, 64·4; H, 5·2; N, 7·8%).

3-(*Piperonylidene*)*guaiazulenium picrate*, red, m. p. 104—105° (decomp.) (Found: C, 62·7; H, 4·6; N, 6·9. $C_{29}H_{25}O_9N_3$ requires C, 62·2; H, 4·5; N, 7·5%).

3-3′-*Bromobenzylideneguaiazulenium picrate*, orange (from formic acid), m. p. 74—75°

(decomp.) (Found: C, 56·6; H, 4·3; N, 7·0; Br, 12·4. $C_{28}H_{24}O_7N_2Br$ requires C, 56·6; H, 4·1; N, 7·1; Br, 13·5%).

When this method was applied to *p*-dimethylaminobenzaldehyde a mixture was always obtained of a chloride, its hydrochloride, and salts of other substances. It was best to add *p*-dimethylaminobenzaldehyde hydrochloride to guaiazulene in methylene chloride, a blue monosalt being obtained pure enough to show clearly the light absorption properties; the picrate mixture could not be resolved.

Piperonaldehyde usually formed a red chloride but in some experiments gave green needles. These were insoluble in ether, but dissolved in ethanol, concentrated hydrochloric acid, and to some extent in water to bright red solutions similar in colour and absorption to the red product (Found: C, 67·5; H, 6·6; Cl, 11·6%). They afforded a red picrate, m. p. 108° (decomp.) (Found: C, 61·9; H, 4·3; N, 7·8%), which appears identical with that from the red chloride. The green compound may be a complex of 3-piperonylideneguaiazulenium chloride with piperonaldehyde and hydrogen chloride (Calc. for $C_{31}H_{30}O_5Cl_2$: C, 67·2; H, 5·4; Cl, 12·8%).

3-3′-*Bromobenzylguaiazulene*.—3-3′-Bromobenzylideneguaiazulenium chloride, freshly prepared from guaiazulene (1·46 g.) and *m*-bromobenzaldehyde (2·04 g.), was added to dry ether (100 ml.) to which lithium aluminium hydride (0·5 g.) was added. A vigorous reaction occurred and the solution became blue. After 30 min., the complex was hydrolysed by the addition of water, and the ether layer was separated. Chromatography showed that the only product (eluted with light petroleum–ether) was 3-3′-*bromobenzylguaiazulene* which crystallised from ethanol in elongated blue plates, m. p. 77—78° (Found: C, 71·7; H, 6·5; Br, 21·9. $C_{22}H_{23}Br$ requires C, 71·9; H, 6·3; Br, 21·8%). The volume of the unit cell of this compound was found by *X*-ray methods to be 934·7 Å$^3$. The observed density was 1·30 g./c.c. and therefore the molecular weight must be $732/n$ where $n$ is the number of molecules per unit cell. This is almost certainly two in this instance from the *X*-ray evidence and it follows that the molecular weight must be 366. That required is 367.

The substance did not form a trinitrobenzene derivative.

3-*Benzylguaiazulene*.—Reduction of benzylideneguaiazulenium chloride, as above and by hydrogenation, gave a hydrocarbon similar in absorption to the substance described above. It did not however crystallise or form a trinitrobenzene derivative. Analysis of liquids in this series have proved unsatisfactory as they were rapidly oxidised.

*Reaction of 3-Benzylideneguaiazulenium Chloride, etc., with Methylmagnesium Iodide*.—A paste of the chloride (from 2 g. of guaiazulene) in ether was added to a solution of methylmagnesium iodide (6 mols.) in ether (150 ml.). A vigorous reaction occurred. The solution became blue; it was boiled for 30 min. and the complex was decomposed with saturated aqueous ammonium chloride. A considerable proportion of the chlorides remained, owing to coating with the reaction complex, and this was removed by filtration before the ether phase was separated. Chromatography was used in the normal way to afford the products.

(i) From 3-benzylideneguaiazulenium chloride the major product, 3-1′-*phenylethylguaiazulene*, was blue ($\lambda_{max.}$ 630 mμ), did not crystallise and decomposed within a few days (Found: C, 90·7; H, 9·1. $C_{23}H_{26}$ requires C, 91·4; H, 8·6%).

(ii) From 3-piperonylideneguaiazulenium chloride a blue green product (1 : 1 light petroleum–benzene), 3-1′-(3 : 4-*methylenedioxyphenyl*)*ethyl-guaiazulene* was obtained. It again did not crystallise but was prepared for analysis by short-path distillation (Found: C, 82·5; H, 7·9. $C_{24}H_{26}O_2$ requires C, 83·2; H, 7·6%).

(iii) After a reaction with 3-3′-bromobenzylideneguaiazulenium chloride a blue compound was eluted with light petroleum. 1-m-*Bromophenylethylguaiazulene* did not crystallise and formed a hard tar after several days (Found: C, 71·8; H, 6·8; Br, 19·4. $C_{23}H_{25}Br$ requires C, 72·4; H, 6·6; Br, 21·0%).

*Reaction of 3-Benzylideneguaiazulenium Chloride, etc., with Phenylmagnesium Bromide*.—The benzylideneguaiazulenium chloride (from 1 g. of guaiazulene) was suspended in dry benzene (20 ml.) and added to a solution of phenylmagnesium bromide (0·05 mole) in ether. The solution became green and after 30 min. was decomposed with water. The ether–benzene phase was treated in the normal way. A liquid blue hydrocarbon fraction (light petroleum–ether) was obtained. An ethanolic solution of trinitrobenzene was added and blue lozenge-shaped crystals, m. p. 179—182°, were deposited (20 mg.) (Found: C, 91·4; H, 8·1; N, 0·0. $C_{28}H_{28}$ requires C, 92·3; H, 7·8%; *M*, 364. $C_{37}H_{40}$ requires C, 91·7; H, 8·3%; *M*, 484). The *hydrocarbon* formed orthorhombic crystals of cell-volume 2919·8 Å$^3$. Its density was

1·10 g./c.c., hence the calculated molecular weight was 1935/*n*. The nature of the crystal suggested that *n* was 4 or, less probably, 8. The molecular weight would therefore be 484 or 242. This excludes the expected guaiazulenyldiphenylmethane and suggests instead the structure 1 : 1-di-3′-guaiazulenyl-1-phenylmethane.

The same method applied to 3-3′-bromobenzylideneguaiazulenium chloride gave a blue product (light petroleum–ether) which did not crystallise and decomposed rapidly. It appeared to be the expected 1-3′-bromophenyl-1-3′-guaiazulenyl-1-phenylmethane (Found: C, 76·3; H, 6·4; Br, 17·0. $C_{28}H_{27}Br$ requires C, 75·7; H, 6·1; Br, 18·1%).

*Reaction of 3-Benzylideneguaiazulenium Chloride, etc., with Potassium Ethoxide.*—To the benzylidene chloride [from the appropriate aldehyde and guaiazulene (1 g.)], suspended in benzene (30 ml.), an excess of potassium ethoxide (0·05 mole) was added. The mixture was shaken occasionally during 24 hr. at room temperature. The blue solution was filtered, to remove unchanged material, and distilled to small volume. Chromatography yielded several fractions.

(i) 3-Benzylideneguaiazulenium chloride gave a crystalline product (light petroleum–benzene, 4 : 1). Further chromatography removed traces of guaiazulene and a green impurity from it. The blue solid (42 mg.) had m. p. 155—158° (Found: C, 90·9; H, 8·1%).

(ii) 3-3′-Bromobenzylideneguaiazulenium chloride reacted almost completely. Chromatography separated guaiazulene and a blue compound (light petroleum–benzene, 2 : 1) from more strongly adsorbed material. The *product* (115 mg.), crystallised from light petroleum–ethanol, had m. p. 190° (varied with the rate of heating) (Found: C, 79·1; H, 7·0; Br, 14·7. $C_{37}H_{29}Br$ requires C, 78·8; H, 7·0; Br, 14·2%).

(iii) 3-Piperonylideneguaiazulenium chloride yielded guaiazulene and a blue compound (light petroleum–benzene, 2 : 1). This crystallised from benzene–ethanol and from ethyl acetate and had m. p. very variable with the rate of heating (Found: C, 85·8; H, 7·4. $C_{38}H_{40}O_2$ requires C, 86·3; H, 7·6%).

(iv) 3-*p*-Anisylideneguaiazulenium chloride gave a similar result. The *product* recrystallised from ethyl acetate (Found: C, 88·0; H, 8·1. $C_{38}H_{42}O$ requires C, 88·7; H, 8·2%).

*Reaction of 3-Benzylideneguaiazulenium Chloride with Potassium Cyanide.*—(*a*) The benzylidene salt from guaiazulene (1 g.) was suspended in benzene (40 ml.). Potassium cyanide (1 g.) in water (10 ml.) was added. The mixture immediately became blue. After 2 hr. solid matter was removed and the benzene phase was prepared for chromatography which separated guaiazulene (5 mg.), a trace of a hydrocarbon ($\lambda_{max.}$ 725 mμ), and a blue compound (benzene) which crystallised from light petroleum–ethanol as purple needles, m. p. 96—97·5° (1·2 g., 80%) (Found: C, 87·5; H, 7·3; N. 4·1. $C_{22}H_{23}N$ requires C, 88·1; H, 7·4; N, 4·5%). The substance proved to be *α-3′-guaiazulenyl-α-phenylacetonitrile*.

(*b*) The benzylidene salt was treated in benzene with dry potassium cyanide (1 g.). The mixture was milled with glass beads for 6 hr., then left overnight at room temperature, filtered, and treated as before. The products were guaiazulene (92 mg.), a blue fraction (light petroleum–benzene, 9 : 1), and another (light petroleum–benzene, 1 : 1). The second fraction (260 mg.), crystallised from light petroleum–ethanol, had m. p. 156—157° and proved to be a *hydrocarbon* (Found: C, 91·5; H, 8·8. $C_{52}H_{56}$ requires C, 91·8; H, 8·2%). The third fraction was the nitrile obtained under aqueous conditions.

The volume of the unit cell of the nitrile was 913 Å$^3$ and the density 1·07 g./c.c. The molecular weight was calculated to be 588/*n*. The most probable value for *n* is 2, hence the molecular weight is 294. The nitrile requires *M* 313.

*Reaction of 3-3′-Bromobenzylideneguaiazulenium Chloride with Potassium Cyanide.*—The same methods were applied as above. Under aqueous conditions a quantity of salt (from 1 g. of guaiazulene) yielded guaiazulene (17 mg.), a blue solid (20 mg.) eluted by light petroleum–benzene (2 : 1), and a second solid eluted by benzene (510 mg.). The first solid was a *hydrocarbon* whose m. p. varied with rate of heating (Found: C, 82·4; H, 7·6; Br, 10·3. $C_{52}H_{55}Br$ requires C, 82·2; H, 7·3; Br, 10·5%). The second was a *nitrile* (also with variable m. p.) which crystallised from light petroleum–ethanol (Found: C, 77·0; H, 6·3; N, 4·1; Br, 12·5. $C_{40}H_{39}N_2Br$ requires C, 76·5; H, 6·3; N, 4·5; Br, 12·7%).

Under anhydrous conditions the products were guaiazulene (53 mg.), the hydrocarbon (83 mg.), and the dinitrile (210 mg.).

*Hydrolysis and Oxidation of Guaiazulenylphenylacetonitrile.*—The nitrile was not hydrolysed by acid to a characterisable product. When phenylguaiazulenylacetonitrile (1·49 g.) was dissolved

in ethanol (100 ml.), and 4% ethanolic sodium hydroxide (50 ml.) was added, the solution immediately became green (red in transmitted light). After 1 hr. the solution was diluted with water and extracted with ether. The extract was treated in the normal way and unchanged nitrile (935 mg.) was separated from an orange band (benzene–ether, 1 : 1) which gave a green solution (red in transmitted light). Dark purple crystals (230 mg.) were obtained (from light petroleum–ethanol) and had m. p. 120—122° (mixed m. p. with 3-*benzoylguaiazulene*, 119—122°) (Found: C, 87·5; H, 7·4. $C_{22}H_{22}O$ requires C, 87·5; H, 7·3%). The monoclinic crystals had a unit cell of volume 1697 Å$^3$ and a density of 1·19 g./c.c. The mass of the unit cell is therefore 1216 and, as $n$ is probably 4, the molecular weight is probably 304. 3-Benzoylguaiazulene requires $M$ 302.

*Hydrolysis and Oxidation of the Dinitrile.*—The method used for the dinitrile (100 mg.) gave unchanged dinitrile and a brown *compound* (80 mg.), orange on alumina, which crystallised from methanol as needles, m. p. 81—82·5° (Found: C, 75·4; H, 7·0; Br, 13·3. $C_{28}H_{27}O_2Br$ requires C, 75·3; H, 6·1; Br, 13·2%).

*Reaction of 2-Methoxybenzylideneguaiazulenium Chloride with Potassium Cyanide.*—The salt (from 0·4 g. of guaiazulene) was added to an aqueous solution of potassium cyanide. A blue colour immediately developed. An ether extract was made, washed with water, dried, and concentrated. A mixture of ethanol (25 ml.) and 10% aqueous sodium hydroxide (25 ml.) was added but there was no colour change. Air was bubbled vigorously through the solution for 30 min. and the mixture was then set aside for 12 hr. An extract was prepared for chromatography. A blue fraction (light petroleum–benzene, 1 : 1) yielded a solid material from which light petroleum extracted a green impurity. The bright blue residue (220 mg.), *α-3′-guaiazulenyl-α-2′-methoxyphenylacetonitrile*, crystallised from ethyl acetate, had m. p. 160° (Found: C, 84·8; H, 7·4; N, 3·8. $C_{24}H_{23}ON$ requires C, 83·9; H, 7·4; N, 4·1%). There was also an orange band (ether) which gave a blue solution (red in transmitted light); no crystals could be obtained from this.

*Reaction of 3-4′-Nitrobenzylideneguaiazulenium Chloride with Potassium Cyanide.*—The salt (from 0·5 g. of guaiazulene) was added to an aqueous solution of potassium cyanide (1 g.). The green material thus produced was extracted into ether and treated in the normal way except that benzene was required for applying the material to the chromatogram. The products included a little guaiazulene and a blue-green fraction (light petroleum–benzene, 1 : 1) which yielded a blue solid (70 mg.), m. p. 205° (Found: C, 83·1; H, 7·5; N, 3·2. $C_{59}H_{62}O_4N_2$ requires C, 82·3; H, 7·0; N, 3·3%). Other fractions yielded no crystals.

*Reaction of 3-Benzylideneguaiazulenium Chloride with p-Chloroaniline and Aniline.*—*p*-Chloroaniline (1·6 g.) was added to a suspension of 3-benzylideneguaiazulenium chloride (from 1 g. of guaiazulene) in benzene (50 ml.). The colour changed to blue within a few minutes and after 30 min. the solution was filtered to remove unchanged material and *p*-chloroaniline hydrochloride. The benzene solution was treated normally. The products were guaiazulene and a second blue fraction (also light petroleum) which was chromatographed again. The *hydrocarbon* (710 mg.) crystallised as pale blue needles, m. p. 125—126°, from light petroleum–ethanol (Found: C, 91·9; H, 8·3; N, 0·0; Cl, 0·0. $C_{11}H_{12}$ requires C, 91·9; H, 8·1%).

Use of aniline gave essentially the same results. The solid product was apparently identical with that above, m. p. 125—127° (Found: C, 90·8; H, 8·5; N, 0·6%).

*Reaction of 3-3′-Bromobenzylideneguaiazulenium Chloride with Aniline.*—The reaction was carried out as above. The products were guaiazulene (106 mg.) and a blue *substance* (light petroleum–benzene, 2 : 1). The latter crystallised as bright blue needles, m. p. 210° (variable with rate of heating), from light petroleum–ethanol (Found: C, 83·7; H, 7·4; N, 0·0; Br, 9·4. $C_{11}H_{12}Br_2$ requires C, 83·3; H, 7·3; Br, 9·3%).

We thank the Department of Scientific and Industrial Research for a grant (to W. L. S.) and the British Petroleum Company for a grant.

CHEMISTRY DEPARTMENT,
THE UNIVERSITY, EDINBURGH, 9.

[*Received, August 12th*, 1957.]

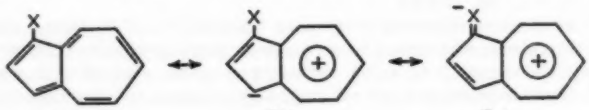
XUM

## 220. *The Azulene Series. Part IV.* The Synthesis and Properties of 3-Acylguaiazulenes.*

By D. H. Reid, W. H. Stafford, and Winifred L. Stafford.

The synthesis and properties of several derivatives of guaiazulene with electron-withdrawing substituents in position 3 are recorded and related to modern concepts of azulene structure.

Derivatives of azulene with electron-attracting groups in position 1 should have properties consistent with a hybrid structure derived from the normal azulene forms [1] (Ia and b), together with the fulvenoid forms represented by (Ic). The last should reduce the importance of (Ib) to which typical azulenic properties have been ascribed.[2] The polarisation indicated by (Ic) should affect reciprocally the characteristic properties of both the azulene portion and the group X. In extreme cases the condition should approach that of the 3-benzylideneguaiazulenium salts described in the previous paper. These predictions have been confirmed by examination of a number of 3-acylguaiazulenes (1-acyl-3 : 8-dimethyl-5-*iso*propylazulenes).



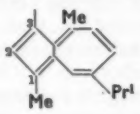
(Ia) (Ib) (Ic)

The Gattermann reaction was employed to prepare 3-formylguaiazulene. A red complex was deposited and decomposition of this yielded unchanged guaiazulene and a basic material retained in the red aqueous phase. On basification this became blue but the resulting blue ether extract became brown on concentration, with evident decomposition. However, the blue solution gave derivatives of the correct composition if the carbonyl reagents were added to it and so contained substantial quantities of the aldehyde.

Two aldoximes were isolated by chromatography and, by analogy with the benzaldoximes, were assigned the α- (II) (34% yield) and the β-stereo-form (III) (<3%) yield respectively; they differed in crystal form, m. p., spectra, and *X*-ray powder diagrams. The α- and β-hydrochlorides were distinct, but both afforded the α-oxime when treated with alkali. A third isomer, spectroscopically identical with the α-oxime, is regarded as a crystalline modification of the latter.

(II) α β (III)

[Gu]³≡3′-Guaiazulenyl



It was not possible to confirm the assignment of configuration by the classical means as the expected nitrile was produced from both forms during the attempted formation of the *O*-acetyl compound. The infrared OH stretching frequencies of the oximes (see Table 1) agree qualitatively, but not quantitatively, with Palm and Werbin's generalisation.[3] The C=N vibrational frequency [4] is higher for the β- than for the α-form, which seems to be true also in many other cases though Palm and Werbin were unable to find this consistency.

* Part III, preceding paper.

[1] Galloway, Reid, and Stafford, *Chem. and Ind.*, 1954, 724.
[2] Stafford and Reid, *Chem. and Ind.*, 1954, 277.
[3] Palm and Werbin, *Canad. J. Chem.*, 1954, **32**, 858; 1953, **31**, 105.
[4] Kahovec and Kohlrausch, *Monatsh.*, 1952, **83**, 614; Duyckaerts, *Bull. Soc. roy. Sci. Liège*, 1952, 196.

TABLE 1. *The infrared absorption frequencies (cm.$^{-1}$) of some 3-substituted guaiazulenes in Nujol.*

| Note | CN | $NO_2$ | CMe:N·OH | α, CH:N·OH | β, CH:N·OH | CMe:N·OH,HCl | α-Oxime, HCl | β-Oxime, HCl |
|---|---|---|---|---|---|---|---|---|
| 1 | — | — | 3175s | 3195s | 3155s | 2551, 2469 s | 2611, 2488 s | 2511s |
| 2 | 2183s | — | — | — | — | — | — | — |
| 3 | — | 1621s | 1619m | 1605m | 1621s | 1639m, 1603s | 1645s, 1592s | 1642s |
| | | 1605w | 1608w | | | | | |
| | 1550m | 1582m | | | | | | |
| 4 | 1534m | — | 1538s | 1543s | 1534m | 1534s | 1534s | — |
| | 1520m | 1526s | 1520m | 1520w | 1520m | | 1527s | 1522m |
| | | | | | | | 1504m | 1506s |
| * | 1412s | 1408s | 1416s | 1408s | 1401s | 1420m | 1431m | 1395s |
| | | | | | | | 1389s | |
| † | 1328m | — | 1330w | 1333w | 1319s | 1333w | 1333s | 1342m |
| * | 1299m | 1299m | 1299w | 1290s | 1294w | 1302w | 1304s | 1309s |
| | | 1230s | | | | 1239w | 1239w | 1232w |
| | | | 1224s | 1217w | | | 1227w | |
| † | 1209m | 1212m | — | 1205m | 1203w | 1203w | 1205m | — |
| | | 1176s | 1198s | 1176s | | | 1195w | 1198m |
| * | 1157s | 1153m | 1166m | 1166s | 1167s | 1147s | 1167s | 1171m |
| * | 1122w | 1124m | 1126w | 1121w | 1120w | 1126w | 1135w | 1139w |
| | 1099m | 1096w | 1104m | 1103w | 1105w | 1100w | 1106w | — |
| † | — | 1073m | 1087w | 1087w | 1085w | 1088m | 1092, 1073m | 1095m |
| * | 1055s | 1054m | 1048s | 1056s | 1049m | 1068s | 1056w | 1058w |
| | | | | | | 1052m | 1042w | 1038w |
| * | | 1031w | | 1027m | | | | |
| | 1019m | 1026m | 1020w | 1016m | 1024m | 1025m | 1018s | 1024w |
| * | 996w | 1002s | 1006s, 984s | 995s | 994w | 1010m, 996m | 998s, 988 | 999m, 990s |
| * | 959w | 955m | 939s | 944s | 954s | 957s | 968s | 968s |
| * | 917m | 941s, 936, 926 | 918s | — | 934s, 915 | 920s | 907m | 933w, 911w |

Notes: 1, OH stretching. 2, C:N stretching. 3, C:O and C:N. 4, Skeletal C:C. * Frequencies to be attributed to 3-guaiazulenyl and its component groups. † Possibly to be attributed as *.

The basic character of these oximes suggested that they would readily form nitrones. However, boiling either the α- or the β-oxime in methyl iodide gave a little guaiazulene, the violet 3-cyanoguaiazulene (IV) (in reasonable quantity), and 3-formylguaiazulene (in small quantity), but no nitrone. 3-Formylguaiazulene, thus produced, was a stable

$$[Gu]^3\cdot CH{=}N\cdot\ddot{O}H + CH_3{-}I \longrightarrow [Gu]^3{-}C{\equiv}N + CH_3\cdot OH + HI$$
(IV)

violet compound, which contrasted with the properties of the ether extract obtained in the Gattermann reaction. It was then found that adding light petroleum (b. p. 80—100°) to the ether extract before its evaporation prevented the decomposition, and chromatography separated the formyl compound from a strongly adsorbed material which decomposed on the column. The yield of aldehyde (17%) contrasted with that for the oxime (37%) from the same extract and it was concluded that a blue, unstable, basic precursor must be present; the aldimine (V) was most likely but it could not be isolated.

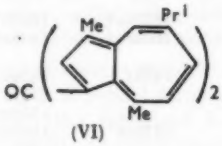
$$Gu\cdot CH{:}NH \xrightarrow{H} Gu\cdot CH{:}NH_2^+ \longleftrightarrow Gu^+{:}CH\cdot NH_2$$
(V) (Gu = 3-guaiazulenyl)

The betaine-type contributing forms for azulene (Ib) were suggested by us on analogy with compounds such as the methine enol-betaines.[5] The latter are acylated by acid anhydrides and halides, and guaiazulene was similarly converted by acetyl bromide into the known 3-acetylguaiazulene[6] without the assistance of Friedel–Crafts catalysts.

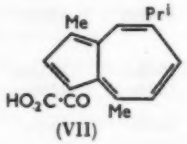
[5] Kröhnke, *Ber.*, 1937, **70**, 1114; 1935, **68**, 1177.
[6] Ukito, Watanabe, and Miyasaki, *J. Amer. Chem. Soc.*, 1954, **76**, 4584.

XUM

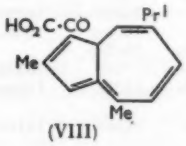
Benzoyl bromide gave a low yield of 3-benzoylguaiazulene, but the yield was also low when a catalyst was used. Oxalyl chloride also reacted swiftly with guaiazulene: if methylene chloride was used as solvent no complex was deposited and di-3-guaiazulenyl ketone (VI) was the only isolable product; in light petroleum the reaction was less complete and a solid complex was precipitated which yielded the ketone (VI) and 3-guaiazulenyl



(VI)

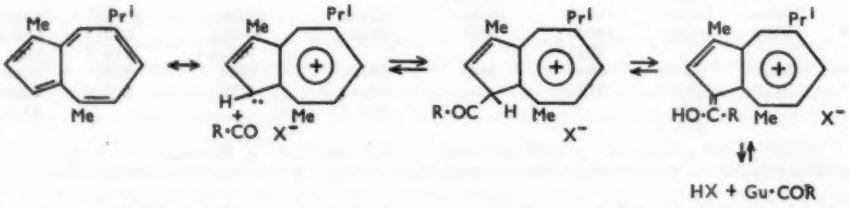


(VII)



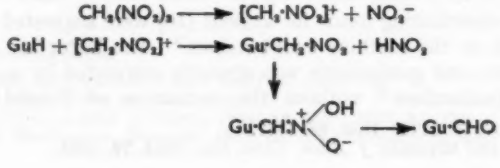
(VIII)

glyoxylic acid (VII). [In one experiment, with a less pure specimen of guaiazulene, an isomeric acid was isolated, which probably has structure (VIII) as the hypsochromic displacement of the visible absorption by 46 mμ relative to (VII) is that expected of a methyl shift from 1 to 2; presence of 2 : 4-dimethyl-7-*iso*propylazulene (*Se*-guaiazulene) in the starting hydrocarbon is not improbable.] Position 1 is preferred to position 3 as the site of reaction because of the probable steric effect of the 4-methyl group. Carbonyl chloride gave the same ketone (VI) and another, red acid. The latter was however not isolated as it was decarboxylated to guaiazulene with great ease. The mechanism of these reactions is interpreted generally as in the annexed scheme. The reactions are regarded




as reversible because all the guaiazulene compounds with electron-withdrawing groups in position 3 give guaiazulene on treatment with acid. Diguaiazulenyl ketone when in hydrochloric acid gives guaiazulene quantitatively within a few minutes. The nitrile, the aldoximes, the benzoyl and the acetyl compound all generate guaiazulene in hot acid. The formyl compound is degraded in acid too quickly for spectroscopic measurements in other than the visible region. This method of acylation without catalyst is probably preferable to the use of stannic chloride, for it has been shown that a dimeric hydrocarbon is produced when guaiazulene and stannic chloride are mixed: this dimer has a visible maximum at 630 mμ, indicating that an alkyl group of one guaiazulene group has reacted with position 3 of the other.

Tetranitromethane with guaiazulene gives 3-nitroguaiazulene and the yield is constant of at least 0·6 mol. of reagent is used. If 0·3 mol. is used guaiazulene remains un-nitrated and is therefore available for a slow reaction with either an impurity in the reagent or with dinitromethane which appears incapable of nitrating guaiazulene; the product isolated, which suggested this secondary process, was 3-formylguaiazulene, possibly formed as in the annexed scheme where the last stage is regarded as analogous to the Nef reaction.



The absorption spectra of the new compounds are recorded in Figs 1—10 and in Table 2, for a non-hydroxylic solvent (hexane when solubility permitted),[7] ethanol and various acidic solvents. Hydrogen-bonding and salt formation caused changes in the absorption spectra interpreted as follows:

| | GuX | GuX···HOR ⟷ Gu⁺–XH···⁻OR | Gu⁺–XH ⟷ Gu=⁺XH |
|---|---|---|---|
| In: | Hexane | Hydroxylic solvents | Acid |

In hexane the absorption spectra give a measure of the interaction of the group X with the characteristically absorbing azulene portion, an interaction represented fundamentally by

FIG. 1. *3-Formylguaiazulene (A) in hexane, (B) in* EtOH.

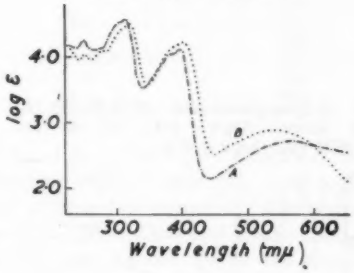



FIG. 2. *3-Formylguaiazulene (A) in* EtOH, *(B) in* 50%-*aq.* EtOH, *(C) in* N-*aq.* EtOH–HCl, *(D) in* 2N-*aq.* EtOH–HCl, *(E) in* 5N-*aq.* EtOH–HCl.

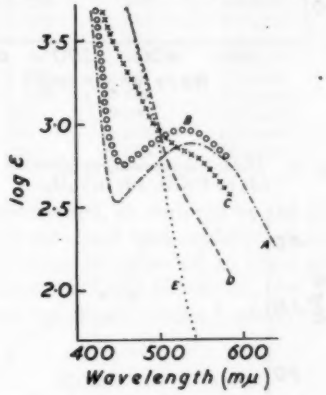



FIG. 3. *3-Benzoylguaiazulene (A) in hexane, (B) in* EtOH, *(C) in* 5N-EtOH–HCl, *and (D) 3-benzylideneguaiazulenium chloride.*

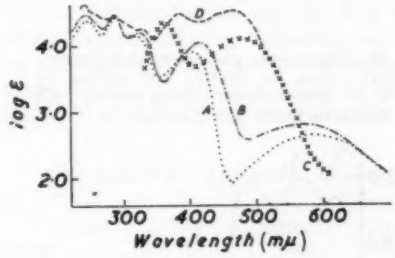
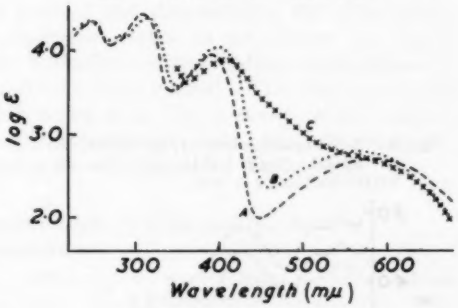



FIG. 4. *3-Acetylguaiazulene (A) in hexane, (B) in* EtOH, *(C) in* 5·5N-EtOH–HCl.




(Ic) but including changes in the contributions of (Ia and b) by processes not involving electron-sharing with X. In Table 2 the results are summarised and four maxima ($A \longrightarrow D$) are considered. It is apparent that *B*, *C*, and *D* suffer bathochromic displacements relative to the parent guaiazulene, but that the shift of *B* is very dependent on X, in the order $CN < COMe < CHO < COPh < COGu < NO_2$. The visible absorption maximum *A* is displaced hypsochromically but here the effect of $NO_2$ and CHO is greater than of

[7] Heilbronner and Schmid, *Helv. Chim. Acta*, 1954, **37**, 2018; Heilbronner and Gerdil, *ibid.*, 1956, **39**, 1996; W. L. Galloway, Ph.D. Thesis, Edinburgh, 1956.

FIG. 5. *3 : 3'-Diguaiazulenyl ketone (A) in hexane, (B) in* EtOH, *(C) in* 2·3N-EtOH–AcOH, *(D) in* 0·5N-EtOH–HCl, *(E) in* 4N-EtOH–HCl.

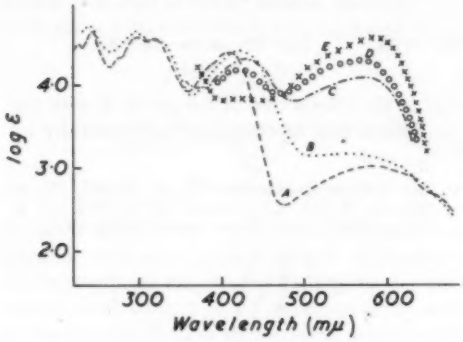



FIG. 6. *3-Guaiazulenylglyoxylic acid (A) in* $C_6H_6$, *(B) in* EtOH, *(C) in* 2N-EtOH–HCl.

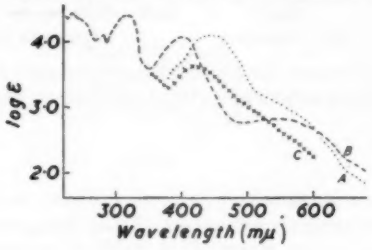



FIG. 7. *Methyl 3-guaiazulenylglyoxylic acid (A) in* EtOH, *(B) in* $C_6H_6$.

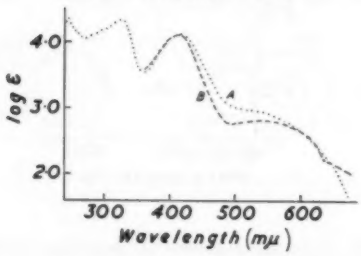



FIG. 8. *3-Cyanoguaiazulene (A) in* EtOH, *(B) in hexane* (log ε + 0·4), *(C) in* 2N-EtOH–HCl (log ε + 0·8).

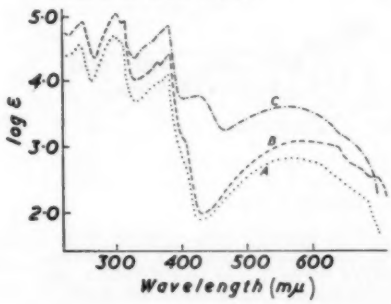



FIG. 9. *3-Nitroguaiazulene (A) in hexane, (B) in* EtOH (log ε + 0·4), *(C) in* 2N-EtOH–HCl (log ε + 0·8).

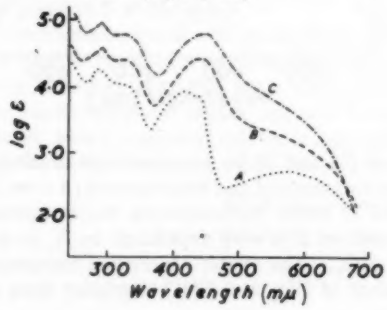
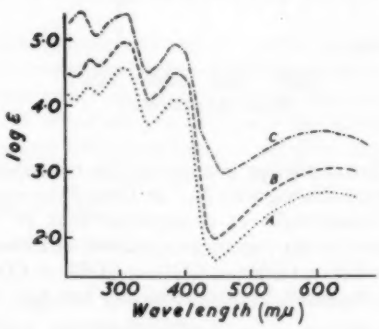



FIG. 10. *The isomeric guaiazulene-3-aldoximes, (A) α-form in* EtOH; *(B) α-form in 9 : 1 hexane*–EtOH (log ε + 0·4), *(C) β-form in* EtOH (log ε + 0·8).

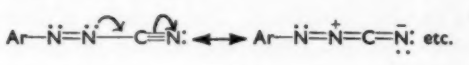


the others. The reciprocal effect of this polarisation change in the light-absorbing azulene portion will be a polarisation of the multiple bond of X demonstrable by the infrared stretching frequencies of there bonds. These are summarised in Table 3. The carbonyl frequencies are comparable and the order of polarisation is COMe < CHO ⩽ COPh < COGu, in reasonable agreement with the relative effects

TABLE 2. *Ultraviolet and visible absorption maxima* (mμ) *of some 3-substituted guaiazulenes in hexane and in ethanol.*

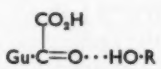
| Subst. | *A* | *B* | *C* | *D* | Solvent |
|---|---|---|---|---|---|
| CHO | 568 | 397 | 314, 276 | 250 | Hexane |
| | 538 | 401 | 318, 279 | 251, 238 | Ethanol |
| COMe | 580 | 390 | 306 | 249 | Hexane |
| | 560 | 397 | 311, 277 | 240 | Ethanol |
| COPh | 583 | 399 | 314, 289 | 249 | Hexane |
| | 566 | 413 | 325, 289 | 240 | Ethanol |
| COGu | 582 | 407 | 316, 298 | 242 | Hexane |
| | 550 | 424 | 313, 297 | 240 | Ethanol |
| CN | 580 | 379, 361 | 312, 298 | 247 | Hexane |
| | 560 | 378 | 310, 298 | 246 | Ethanol |
| α-CH:N·OH | 625 | 385 | 308 | 257 | Hexane |
| | 620 | 385 | 308 | 254 | Ethanol |
| H | 605 | 367, 350 | 285 | 246 | Hexane |

on band *B*. The values indicate a high degree of polarisation, as required by the hybrid structure derived from (Ia, b, and c). The nitro-, cyano-, and hydroxyimino-group are also polarised as expected. The normal absorption frequencies expected for these groups are $NO_2$ 1560—1500 and 1350—1300 cm.$^{-1}$, CN *ca.* 2230 cm.$^{-1}$, and HO·N= *ca.* 1640 cm.$^{-1}$. In the case of the nitrile the closest analogues are the diazocyanides [8] which have a polarised structure (IX).




(IX)

(Xa)




(Xb)

The influence of hydroxylic solvents is marked and demonstrates the polarisability of the system. The general form of the absorption curves do not change but band *A* shifts hypsochromically and band *B* shifts bathochromically. 3-Guaiazulenylglyoxylic acid is exceptional in its behaviour but its methyl ester is normal. This can be explained by postulating the intramolecular hydrogen-bonding as in (Xa) in non-polar solvents and a weaker intermolecular bonding to hydroxylic solvents (cf. Xb). The infrared spectra (Table 3) of the carbonyl compounds in ethanol show the expected displacement.

TABLE 3. *Infrared stretching frequencies* (cm.$^{-1}$) *of the multiple bond in 3-acylguaiazulenes.*

| Subst. | $CCl_4$ | EtOH | Nujol | KBr |
|---|---|---|---|---|
| Acetyl | 1674, 1658 | 1650 | — | — |
| Formyl | 1634 | 1614 | — | 1618 |
| Benzoyl | — | — | 1637 | — |
| Guaiazuloyl | 1616 | 1594 | — | — |

| Subst. | Nujol |
|---|---|
| α-Formyl oxime | 1605 |
| β-Formyl oxime | 1621 |
| Acetyl oxime | 1629 |
| Cyano | 2183 |
| Nitro | 1526, 1230 |

In acid solution salt formation generally occurs and the absorption changes radically. In most instances where the formation of a cation is complete, the normal visible absorption *A* disappears, as does band *B*, to be replaced by a single band of high intensity.

[8] Sheppard and Sutherland, *J.*, 1947, 453.

XUM

Investigation of the ultraviolet region was impossible owing to rapid degradation. In two instances the effects of different degrees of acidity on the absorption in the visible region have been studied. In Fig. 2 band *A* for the aldehyde is recorded in ethanol, 50% aqueous ethanol, and 50% aqueous ethanol containing 3 concentrations of hydrochloric acid. Introduction of water causes a normal hydrogen-bonding effect—hypsochromic translation of *A*. As the acidity increases there is evidence of an equilibrium involving the cation and the neutral substance, which progressively favours the former with the disappearance of band *A*. In the second instance, Fig. 5, 3 : 3′-diguaiazulenyl ketone in 5 solvents, high acid concentrations produce a permanganate colour but band *B* decreases in intensity and a new band which coincides with *A* increases rapidly. In these two instances virtually complete production of the cation can be achieved, but in some of the other compounds the change is less complete.

The benzoyl compound (Fig. 3) demonstrates a parallelism between the resulting cation (XIa) and the 3-benzylideneguaiazulenium salts (XIb). There is, in the visible region at least, some similarity in form. When 3-formylguaiazulene reacted with guaiazulene in the presence of hydrogen chloride, the resulting blue compound (XIIa) was unstable but its visible absorption maximum was very similar to that of the cation (XIIb) (formed from diguaiazulenyl ketone in acid) both in intensity and position. This intense absorption was also found in the blue 3-*p*-dimethylaminobenzylideneguaiazulenium chloride which although not obtained pure was shown to have a visible absorption maximum fifty times more intense than that of guaiazulene.

$$\underset{\text{(XIa)}}{\text{Gu}^{+}\!:\!\text{CR}\cdot\text{OH}} \qquad \underset{\text{(XIb)}}{\text{Gu}^{+}\!:\!\text{CHR}} \qquad \underset{\text{(XIIa)}}{\text{Gu}\cdot\text{CH}\!:\!\text{Gu}^{+} \longleftrightarrow \text{Gu}^{+}\!:\!\text{CH}\cdot\text{Gu}} \qquad \underset{\text{(XIIb)}}{\text{GuC(OH)}\!:\!\text{Gu etc.}}$$

The absorption spectra discussed above agreed well with expectation, but the oximes were divergent (Fig. 10). A bathochromic shift of both bands *A* and *B* occurs and the shift in *A* is slightly less than that due to an alkyl substituent. Any donation of electrons to the azulene moiety, which might explain this shift, would also increase the acidity of the hydroxyimino-group, which is not observed.

Some reactions of these acyl compounds were studied. Attempts to prepare alcohols from 3-formyl- and 3-acetyl-guaiazulene by means of phenylmagnesium bromide or lithium aluminium hydride failed. It appears that nucleophilic reagents attacked the azulene nucleus. However, lithium aluminium hydride reduced the glyoxylic acid to the glycol (XIII); this dissolved in acid to give presumably the yellow salt (XIV), but within a few minutes decomposition occurred and blue material was re-extractable into ether; the blue material had carbonyl reactivity but no pure derivative could be isolated.

The base-catalysed condensation of 3-acetylguaiazulene with benzaldehyde gave no crystalline product, but a material with the characteristic chromatographic behaviour of an acylazulene was separated. An alternative attempt to synthesise 3-cinnamoylguaiazulene from guaiazulene and cinnamoyl bromide gave a similar material. Attempts to

$$\underset{\text{(XIII)}}{\text{Gu}\cdot\text{CH(OH)}\cdot\text{CH}_2\cdot\text{OH}} \longrightarrow \underset{\text{(XIV)}}{\text{Gu}^{+}\!:\!\text{CH}\cdot\text{CH}_2\cdot\text{OH}} \longrightarrow \text{Gu}\cdot\text{CH}_2\cdot\text{CHO}$$

prepare 2-3′-guaiazulenylquinoline by the reaction of 3-acetylguaiazulene and *o*-aminobenzaldehyde gave a gummy product in low yield. Salicylaldehyde under acid conditions gave an unstable dark red product which may have been the oxonium salt but neither it nor a derivative could be obtained pure.

3-Cyanoguaiazulene also failed to react with methylmagnesium iodide in very large excess. Methyl iodide and 3-acetylguaiazulene oxime gave at least three products, which were very unstable and were not obtained pure; they appeared to be basic and one on decomposition gave methylamine.

XUM

Both 3-formyl- and 3-acetyl-guaiazulene gave normal ketonic derivatives but 3-benzoylguaiazulene and 3 : 3′-diguaiazulenyl ketone did not react with hydroxylamine or dinitrophenylhydrazine. The phenylhydrazone of the acetyl compound was a liquid and was obtained analytically pure; it did not give 2-3′-guaiazulenylindole on treatment with acid.

## Experimental

The procedure for chromatography was as in Part III and the guaiazulene used was commerical " Azulen " made by Dragoco Ltd.

*3-Formylguaiazulene.*—A suspension of zinc cyanide (5·9 g.) in a dry ethereal solution (50 ml.) of guaiazulene (5·0 g.) was saturated with hydrogen chloride. A red complex was deposited, which after 15 hr. was decomposed with dilute hydrochloric acid, repeated warming with methylene chloride and concentrated hydrochloric acid being required to effect dissolution. The red aqueous phase was separated from the blue ether phase, exhaustively extracted with ether to remove guaiazulene, and made alkaline with aqueous sodium hydroxide, and the precipitated blue material was taken into ether. The ether extract was dried ($Na_2SO_4$), light petroleum (b. p. 80—100°) was added, and the ether distilled off. Dissolved material decomposed at the end of the distillation. The residual solution was chromatographed. Elution with benzene containing a little ether separated a brown band from a strongly adsorbed green band. The purple eluate gave dark red needles (from ethanol), m. p. 84—84·5°. The *formyl compound* (Found: C, 84·7; H, 7·9. $C_{16}H_{18}O$ requires C, 84·9; H, 8·0%), obtained in 17·6% yield, formed a 2 : 4-*dinitrophenylhydrazone* as red needles (from glacial acetic acid), m. p. 285° (decomp.) (Found: C, 66·0; H, 5·5; N, 13·3. $C_{22}H_{22}O_4N_4$ requires C, 65·0; H, 5·5; N, 13·8%).

An ethereal solution of the formyl compound gave 3-*hydroxymethyleneguaiazulenium chloride* on saturation with hydrogen chloride. This could not be recrystallised and analysis showed that it was a hydrate (Found: C, 68·5; H, 7·7; Cl, 12·7. $C_{16}H_{21}O_2Cl$ requires C, 68·4; H, 7·5; Cl, 12·7%).

*Oximes.* (*a*) 3-Formylguaiazulene (50 mg.) was dissolved in ethanol (10 ml.) containing 10% aqueous sodium hydroxide (4 drops). Hydroxylamine hydrochloride (250 mg.) was added and the solution was boiled for 30 min. The blue solution was diluted with water and an ether extract was treated normally. Chromatography yielded a trace of yellow material (ether), and a mixture of the two oximes as a green solution (ether–ethanol, 7 : 1). The solution was taken to dryness and the residue was re-chromatographed, to give two oximes, *form A* as green plates (from light petroleum–ethanol), m. p. 128—130° (Found: C, 79·4; H, 8·0; N, 6·0. $C_{16}H_{19}ON$ requires C, 79·6; H 7·9; N, 5·9%), and *form B* as green needles (from ether–light petroleum), m. p. 162° (Found: C, 79·2; H, 7·9; N, 5·8%). The total yield (40 mg., 80%) of the isomers contained only 5% of form B.

(*b*) To the crude extract from the preparation of the formyl compound, ethanolic hydroxylamine hydrochloride, made just alkaline with 10% aqueous sodium hydroxide, was added and the ether was removed. The above procedure was then followed. No aldehyde remained and a 37% yield of oximes with respect to the guaiazulene was obtained.

(*c*) The *hydrochloride* was prepared by passing hydrogen chloride into an ethereal solution of form A. The red solid initially precipitated became partly purple on the filter. The mixed solid, m. p. 135—145° (decomp.), was analysed in the crude state (Found: C, 68·6; H, 6·2; N, 4·7; Cl, 11·6. Calc. for $C_{16}H_{20}ONCl$: C, 69·1; H, 7·3; N, 5·0; Cl, 12·8%). Freshly prepared hydrochloride of form A was decomposed with 5% sodium hydroxide solution and extracted into ether. The extract was treated normally and chromatography separated a small quantity of form A, m. p. 125°, from a large quantity of form B which crystallised as green needles. m. p. and mixed m. p. 162°.

The *hydrochloride* of form B, similarly prepared, formed purple crystals, m. p. 138—140° (decomp.) (Found: C, 69·4; H, 7·3; N, 5·0; Cl, 12·4%). Decomposition of the hydrochloride of form B with alkali yielded only form B of the oxime.

*Hydrolysis of oxime A.* The oxime (50 mg.) was heated in ethanol (10 ml.) containing 10% aqueous hydrochloric acid (10 ml.) for 40 min., cooled, and extracted with ether. The extract on normal treatment yielded guaiazulene.

*Action of Methyl Iodide on 3-Formylguaiazulene Oximes.*—A solution of oxime A (586 mg.)

in methyl iodide (25 ml.) was boiled for 30 min. The residue, after removal of methyl iodide, was chromatographed, yielding (i) a little guaiazulene, (ii) a purple solution (benzene–ether, 7 : 3), and (iii) an orange band eluted as a purple solution (ether). The compound (ii) crystallised from ethanol and was sublimed under reduced pressure. *3-Cyanoguaiazulene* (75 mg., 13·8%) is very soluble in all organic solvents (Found: C, 85·7; H, 7·8; N, 6·8. $C_{16}H_{17}N$ requires C, 86·1; H, 7·7; N, 6·3%). The eluate (iii) yielded 3-formylguaiazulene (10 mg., 1·8%), m. p. 84–84·5°, confirmed by mixed m. p., analysis, and absorption spectrum. 40% of the α-aldoxime was recovered.

The same products were obtained from form B.

*3-Acetylguaiazulene.*—Acetyl bromide (0·7 ml.) was added to guaiazulene (0·777 g.) in light petroleum (0·8 ml.; b. p. 60—80°) and the solution was left for 24 hr. The brown complex was treated with 1 : 1 aqueous ethanol (20 ml.), and the solution was extracted with ether and treated normally. The first eluate (light petroleum) was green and from it the guaiazulene trinitrobenzene derivative was isolated (m. p. and analysis), leaving bright yellow mother-liquors. The yellow material was unstable to further chromatography. A second product (eluted with benzene) was rechromatographed and crystallised from light petroleum–ethanol as purple plates, m. p. 85·5—86° (349 mg., 37%) (Found: C, 84·6; H, 8·2. $C_{17}H_{20}O$ requires C, 85·0; H, 8·5%). *3-Acetylguaiazulene* formed a red trinitrobenzene derivative, m. p. 124°, and a red 2 : 4-di-*nitrophenylhydrazone*, m. p. 109—110·5° (Found: C, 65·7; H, 5·7; N, 13·9. $C_{23}H_{24}O_4N_4$ requires C, 65·7; H, 5·7; N, 13·3%).

Use of weaker solutions in light petroleum led to lower yields but when methylene chloride (6 ml.), guaiazulene (0·8 g.), and acetyl bromide (0·75 g.) were employed the yield of ketone was 43%.

Acetylguaiazulene (100 mg.) was heated in trichloroacetic acid (1 g.) at 60° for 1 hr., added to dilute ammonia solution, and extracted with ether. The extract was treated normally, yielding guaiazulene (*ca.* 60 mg.) and brown decomposition products.

Phenylhydrazine (0·5 g.) and 3-acetylguaiazulene (200 mg.) in 10% ethanolic acetic acid (10 ml.) were warmed for a few minutes, then cooled and filtered. The filtrate was poured into water, and an ether extract was prepared. Chromatography yielded a blue-green compound which did not crystallise. The liquid *phenylhydrazone* was analysed (Found: C, 83·7; H, 4·1; N, 8·5. $C_{23}H_{26}N_2$ requires C, 83·7; H, 7·8; N, 8·5%).

A solution of 3-acetylguaiazulene (550 mg.) and hydroxylamine hydrochloride (240 mg.) in pyridine (80 ml.) was boiled for 75 min. More hydroxylamine hydrochloride (330 mg.) was then added and heating continued for 30 min. The solution was poured into water, and an ether extract was made, washed with dilute hydrochloric acid, and prepared for chromatography. Acetylguaiazulene (eluted with benzene) was separated from a blue compound (eluted with ether). The latter crystallised as blue plates (from light petroleum–ethanol), m. p. 140—141·5°, and proved to be a single *oxime* (245 mg., 42%) (Found: C, 79·7; H, 8·3; N, 5·5. $C_{17}H_{21}ON$ requires C, 80·0; H, 8·3; N, 5·5%). This formed a *hydrochloride*, red needles, m. p. 110—120° (decomp.), which were analysed in the crude state (Found: C, 69·7; H, 8·8; N, 4·2; Cl, 11·7. $C_{17}H_{22}ONCl$ requires C, 69·9; H, 7·6; N, 4·8; Cl, 12·2%).

*3-Benzoylguaiazulene.*—Guaiazulene (9·78 g.) was treated in light petroleum (60 ml.; b. p. 60—80°) with benzoyl chloride (10·4 g.) and aluminium chloride (13·5 g.). A red complex was formed with evolution of heat. The mixture was boiled for 15 min. and the complex decomposed by dilute hydrochloric acid. An extract with light petroleum was treated normally. Chromatography gave a brown band, eluted as a blue-green solution by light petroleum which gave a little 3-benzoylguaiazulene and guaiazulene on rechromatography. The major quantity of the ketone came from a benzene–ether (1 : 1) eluate which was green in reflected light and red in transmitted light. *3-Benzoylguaiazulene* forms violet crystals, m. p. 120—121°, from light petroleum–ethanol (Found: C, 87·0; H, 7·0. $C_{22}H_{22}O$ requires C, 87·5; H, 7·3%) (yield, 1·5 g., 10%). The substance formed no ketonic derivatives and no trinitrobenzene derivative.

The ketone was also made by boiling guaiazulene (0·571 g.) and benzoyl bromide (0·82 ml.) in light petroleum (8 ml.; b. p. 80—100°) for 4·5 hr. The complex was decomposed with 50% aqueous ethanol, and an ether extract was prepared and treated normally. A good return of guaiazulene, together with 3-benzoylguaiazulene (70 mg., 8%), was obtained.

*Action of Oxalyl Chloride on Guaiazulene.*—(*a*) Oxalyl chloride (0·29 g.) was added dropwise to a solution of guaiazulene (0·46 g.) in methylene chloride (5 ml.). After 2 hr. the reddish-purple solution was diluted with ether and washed free from acid. No azulenic acid was

XUM

present. The extract was treated normally and chromatography yielded guaiazulene (0·13 g., 28%; eluted with light petroleum) and a brown band (eluted with benzene) from which 3 : 3′-*diguaiazulenyl ketone* was obtained as dark green needles (70 mg., 14·3%), m. p. 189—191° (from ethanol) (Found: C, 87·5; H, 8·1. $C_{31}H_{34}O$ requires C, 88·1; H, 8·1%).

(*b*) Oxalyl chloride (305 mg.) was added to guaiazulene (480 mg.) in light petroleum (5 ml.; b. p. 60—80°). The solvent became red with slow evolution of gas and a brown solid was deposited. The mixture was treated with water after 2½ hr. at room temperature and an ether extract was made. This was washed with water until extraction of acid was complete and the now orange ethereal extract was treated as above, yielding 3 : 3′-diguaiazulenyl ketone (75 mg., 14·7%). The aqueous extracts were acidified and extracted with ether. The last-mentioned ethereal extract was extracted with successive small portions of 2N-sodium hydroxide. The combined alkaline solutions were washed once with ether and acidified with concentrated hydrochloric acid. The 3-*guaiazulenylglyoxylic acid* was removed by filtration after 2 hr. at 0°. It formed reddish-brown needles, m. p. 115—116° (150 mg., 22·9%), from ether (Found: C, 75·5; H, 6·7. $C_{17}H_{18}O_3$ requires C, 75·5; H, 6·7%), and formed with diazomethane a *methyl ester*, in the normal way. The ester formed red plates, m. p. 97·5—98° (from acetone–light petroleum, 1 : 3) (Found: C, 76·0; H, 7·0. $C_{18}H_{20}O_3$ requires C, 76·1; H, 7·1%).

In an early experiment a red water-soluble acid, isolated in low yield, was perhaps 2 : 4-*dimethyl*-7-iso*propyl*-1-*azulenylglyoxylic acid*, m. p. 125—129°, with an absorption at 500 mμ (Found: C, 75·5; H, 6·8. $C_{17}H_{18}O_3$ requires C, 75·6; H, 6·7%).

3-(1 : 2-*Dihydroxyethyl*)*guaiazulene*.—The 3-glyoxylic acid (270 mg.) in ether (50 ml.) was treated for 1 hr. with lithium aluminium hydride (100 mg.), then with water, and the blue ethereal layer was separated. It gave the *glycol* as cornflower-blue needles, m. p. 116—118° (variable with rate of heating) (Found: C, 78·9; H, 8·8. $C_{17}H_{22}O_2$ requires C, 79·1; H, 8·6%).

3-*Nitroguaiazulene*.—Guaiazulene (200 mg.) in carbon tetrachloride (20 ml.) was treated dropwise with tetranitromethane (200 mg.) in the same solvent at <5°. Immediate colour change to brown occurred. After 30 min. the solvent was removed and the residue chromatographed. The *nitro-compound* (61 mg., 25%) (eluted with benzene–ether, 9 : 1) crystallised in brown plates, m. p. 72°, from light petroleum (Found: C, 74·2; H, 7·3; N, 5·6. $C_{15}H_{17}O_2N$ requires C, 74·1; H, 7·0; N, 5·8%). The same yield was obtained by using 0·6 mol. of tetranitromethane (120 mg.). When tetranitromethane (60 mg.) was treated as above with guaiazulene (200 mg.) the colour changed only to green and chromatography yielded guaiazulene (37 mg.), 3-nitroguaiazulene (52 mg.), and 3-formylguaiazulene.

*Action of Stannic Chloride on Guaiazulene*.—Solutions of stannic chloride (3 ml.) and guaiazulene (3·0 g.) in light petroleum (15 ml.; b. p. 40—60°) were mixed. The blue colour disappeared rapidly and a yellow complex was deposited which changed to a blue-grey solid during 24 hr. Decomposition with water was followed by extraction with methylene chloride. The extract was washed, dried, and evaporated, and the residue was taken into hot ethanol and freed from unchanged guaiazulene by treatment with *s*-trinitrobenzene (500 mg., 2 × 200 mg.). Impure guaiazulene–trinitrobenzene complex was deposited. The mother-liquors were taken to dryness and the residue was extracted with boiling light petroleum (b. p. 80—100°) until the solid residue was colourless. The combined extracts deposited a little trinitrobenzene on cooling but were freed completely from it by percolation through a small alumina column. The eluates on concentration and cooling deposited violet-black prisms, m. p. 140·5—142° (1·25 g.), which proved to be a *hydrocarbon* (Found: C, 91·2; H, 7·9. $C_{30}H_{34}$ requires C, 91·4; H, 8·6%).

We thank the British Petroleum Co. Ltd. for a grant, also the Department of Scientific and Industrial Research for a grant (to W. L. S.).

CHEMISTRY DEPARTMENT,
THE UNIVERSITY, EDINBURGH, 9.

[*Received, August 12th*, 1957.]

XUM

## 221. *Aluminium Phosphates. Part II.* Ion-exchange and pH-Titration Studies of Aluminium Phosphate Complexes in Solution.*

By J. E. Salmon and J. G. L. Wall.

The sorption of aluminium, phosphate, and chloride from solution by both cation- and anion-exchangers has been studied in batch experiments. The extent of sorption of phosphate (together with aluminium) by the cation-exchanger was found to be dependent both on the pH and on the mole ratio of phosphate to aluminium in the solutions. Sorption of aluminium (together with phosphate) by the anion-exchanger was negligible when chloride was present. These results, together with those of further batch experiments with the aluminium form of the cation-exchanger and those of pH titration experiments, have been interpreted in terms of the formation of complex phosphatoaluminium cations and anions, which are probably less stable than the corresponding ferric phosphate complexes. Some at least of the cationic complexes are binuclear, or polynuclear, and on this basis an explanation is offered of the difficulties encountered by Bjerrum and Dahm [1] in their calculations. No evidence of mixed chlorophosphato-aluminium complexes was found.

From their conductivity and pH measurements on solutions containing aluminium chloride and sodium dihydrogen phosphate Bjerrum and Dahm [1] found evidence for the formation of various phosphatoaluminium complexes which they assumed to be of the types $[Al(H_2PO_4)]^{2+}$, $[Al(HPO_4)]^{+}$, $[Al(H_2PO_4)_2]^{+}$, $[Al(HPO_4)_2]^{-}$, $[Al(HPO_4)_3]^{3-}$, etc. Nevertheless, their attempts to determine the complexity constants led to values which were not compatible with assumptions made. However, Jensen's measurements [2] of the solubility of aluminium tertiary phosphate in acid solutions containing phosphate and chloride indicated that pure phosphato-complexes only were formed in such solutions and that chlorophosphato-complexes were absent.

In their ion-exchange studies of aluminium phosphate solutions in phosphoric acid, Jameson and Salmon [3] found evidence for anionic complexes such as $[Al(HPO_4)_3]^{3-}$, which they believed to be the predominant one, and $[Al(HPO_4)_2]^{-}$—both of the type postulated by Bjerrum and Dahm.

From their ion-exchange and pH-titration studies Holroyd and Salmon [4] deduced that complex formation with phosphate was marked with several tervalent metals, including iron and aluminium, but, on the basis of conductivity measurements, Dede [5] concluded that the aluminium phosphate complexes were less stable than those of ferric phosphate.

A full knowledge of the nature of the aluminium phosphate complexes was evidently lacking and studies similar to those made of the ferric phosphate system [6] were accordingly undertaken.

### Experimental

*Procedure.*—The experimental procedures were those previously described for ion-exchange [3, 6, 7] and pH-titration experiments.[4, 6] Where the aluminium or zinc forms of the cation-exchanger were used, these were prepared by the passage through a column of the exchanger of an excess of a solution of a salt of the metal. The metal was washed thoroughly and allowed to dry in the air. Samples (0·500 g.) were shaken with 50 ml. portions of acid solutions of known pH, and the proportion of metal that had passed into solution at equilibrium

* Part I, *J.*, 1954, 4013.

[1] Bjerrum and Dahm, *Z. phys. Chem.*, Bodenstein Festband, 1931, 627.
[2] Jensen, *Z. anorg. Chem.*, 1934, **221**, 1.
[3] Jameson and Salmon, *J.*, 1954, 4013.
[4] Holroyd and Salmon, *J.*, 1956, 269.
[5] Dede, *Z. anorg. Chem.*, 1922, **125**, 28.
[6] Salmon, *J.*, 1953, 2644.
[7] Genge and Salmon, *J.*, 1957, 256.

XUM

was determined. The total amount of metal present initially in the resin phase was determined by elution of the metal from separate samples of the same batch of resin by an excess of acid and estimation of metal in the eluate. This value was checked against the hydrogen ion capacity [6] of the same samples.

*Materials.*—The aluminium chloride solutions were prepared from aluminium metal of high (spectrographic) purity and hydrochloric acid of analytical grade. All other materials were of analytical grade. The resins used were Zeo-Karb 225 and Amberlite I.R.A. 400, the phosphate form of which was prepared by a method already given.[8]

*Analytical Methods.*—Aluminium was determined gravimetrically by means of 8-hydroxyquinoline (" oxine "). Interference by phosphate was avoided as follows: the acid solution containing aluminium and phosphate was made just alkaline to phenolphthalein by the dropwise addition of M-sodium hydroxide; the solution was heated to 40° and a 10% excess of alcoholic " oxine " reagent was added, followed by 25 ml. of 2M-ammonium acetate; precipitation was completed by heating the suspension to 100° for a short while.

Phosphate was determined by weight as ammonium phosphomolybdate, and chloride gravimetrically as silver chloride.

## Results

*Ion-exchange Experiments.*—The moles of aluminium and phosphate sorbed per equivalent of Zeo-Karb 225 ($N_{Al}$ and $N_{phosphate}$ respectively) from mixtures of aluminium chloride solutions with phosphoric acid or sodium dihydrogen phosphate solutions—or mixtures of all three—are shown in Table 1. No phosphate was sorbed from the solutions of lowest pH, which were obtained with the mixtures of aluminium chloride and phosphoric acid solutions (Table 1*a*), but at the higher pH values obtained with the mixed solutions of aluminium chloride and sodium dihydrogen phosphate (Table 1*b*) a significant sorption of phosphate was observed. This sorption of phosphate reached a maximum when the mole ratio of $PO_4$ : Al in the solution was about 1·5 : 1 (at a mole ratio of $PO_4$ : Al = 6 : 1 it had fallen to 0·013 mole of $PO_4$ per equiv. of resin and the sorption of Al to 0·171 mole/equiv.). The sorption of phosphate was accompanied by an increased sorption of aluminium, which also passed through a maximum at the same mole ratio ($PO_4$ : Al = 1·5 : 1, approx.). The effects of changes in pH of the solutions on the sorptions of both phosphate and aluminium are shown in Table 1*c*. No chloride was sorbed by the cation-exchanger and even when aluminium chloride and phosphoric acid solutions of 2M-concentration were mixed in equal proportions (pH of solution = 0·12) only a trace of chloride was sorbed by the cation-exchanger when in equilibrium with the mixture.

No aluminium was sorbed by the chloride form of the anion-exchanger from mixtures of 0·1M-aluminium chloride with either phosphoric acid or sodium dihydrogen phosphate solutions (Table 2*a*, *b*) and the sorption of phosphate was slight. With the more concentrated solution (Table 2*c*) a slight, but significant, sorption of aluminium occurred and this was accompanied by an increase in phosphate sorption.

For solutions of any pH in the range 0·05—1·25, aluminium was removed from the aluminium form of Zeo-Karb 225 most readily by phosphoric acid, while hydrochloric, sulphuric, and perchloric acid were progressively less effective (Fig. 1*a*). With the zinc form of the resin, however, the metal was removed most readily by hydrochloric acid and, in this case, phosphoric acid was hardly more effective than perchloric acid.

pH-*Titration Experiments.*—The results of the pH-titration experiments with 0·1M-aluminium chloride and nitrate solutions are shown in Fig. 2*b*, together with the previous results for aluminium sulphate,[4] for purposes of comparison, and those of a similar solution to which ammonium sulphate had been added. The increases in hydrogen-ion concentration ($\Delta[H^+]$) over that of the initial solution are recorded in Fig. 2*a* as a plot of $\Delta[H^+]/[Al]$ against the mole ratio in solution of $PO_4$ : Al (cf. refs. 4 and 6).

Additions of sodium chloride or nitrate (to give a concentration, in the solution to be titrated, of up to 0·5M of the salt added) had little effect on the course of the pH-titration beyond causing a very slight increase in release of hydrogen ions (not shown in Fig. 2, but pH fell about 0·05 unit over the whole titration), but addition of sodium sulphate (0·5M) to the aluminium nitrate solution or of ammonium sulphate (Fig. 2) led to a markedly smaller release of hydrogen ions throughout the titration.

[8] Salmon, *J.*, 1952, 2316.

## Discussion

The fact that no complex ions are sorbed by the cation exchanger from the aluminium chloride–phosphoric acid solutions (Table 1*a*) provides a striking contrast with the results obtained with the ferric chloride–phosphoric acid solutions,[6,9] from which sorption of phosphate, in the form of $FeHPO_4^+$ ions, occurred at pH values (0·74—0·79) appreciably lower than those recorded in Table 1*a*. Further, the resin appears to be saturated with aluminium ions [*i.e.*, $N_{Al} = 0{\cdot}33$; the higher values found experimentally (Table 1*a*) will be discussed below] and hence it may be deduced that the extent of complex formation with phosphate is not sufficient to displace the reaction:

$$\overline{Al^{3+}} + 3H^+ \rightleftharpoons Al^{3+} + \overline{3H^+} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

to the left (where barred symbols refer to ions in the resin phase) by a significant extent by lowering the concentration of free aluminium ions in solutions. Thus in this range of pH values the aluminium phosphate complexes are evidently less stable than the ferric ones.

At the higher pH values obtained with the aluminium chloride–sodium dihydrogen phosphate solutions the sorptions of phosphate and aluminium which occur resemble those previously observed for iron and phosphate [6,9] and both pass through a maximum as the proportion of phosphate in solution is increased. As in the ferric chloride–phosphoric acid system at the higher pH values [9] the amounts sorbed are not consistent with the assumption of the sorption of monomeric complex ions. Now for the sorption of a complex ion together with free metal ions it has been shown that the following equation will apply: [9,10]

$$pN_{Al} - qN_{phosphate} = 1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $p$ is dependent on the charge on the free metal ions only, while $q$ depends on $p$ and on both the charge and composition of the complex ion. While $p$ is 3 ideally in the case of aluminium, the values obtained experimentally—from $p = (1/N_{Al})$ when $N_{phosphate} = 0$—are always less than this (Table 1*a* and first values in Tables 1*b* and *c*). Evidently the "free" ions are sorbed as a mixture of $Al^{3+}$aq. and hydroxylated species [*e.g.*, $Al(OH)^{2+}$] in such proportions as to give a mean value of $p$ which is just below 3. Since $p$ appears to be close to a mean value of 2·90 over a wide range of pH, this value has been used in determining the values of $q$ obtained from the experimental results by means of equation 2 (Table 1*b*, *c*).

As an example of the calculation of the values of $q$ for the various possible complexes quoted in Table 1, which are again based on $p = 2{\cdot}9$, that for the complex $[Al_2(PO_4)]^{3+}$ may be considered; where moles complex/equiv. exchanger $= N_{phosphate}$, and moles free Al/equiv. exchanger $= N_{Al} - 2N_{phosphate}$ (*i.e.*, total Al less Al present in the complex which contains two Al atoms per $PO_4$ group). Hence equivs. complex/equiv. exchanger $= 3N_{phosphate}$, equivs. free Al/equiv. exchanger $= 2{\cdot}9(N_{Al} - 2N_{phosphate})$, and total equivs. present $= 1 = 2{\cdot}9N_{Al} - 2{\cdot}8N_{phosphate}$, so that $q = 2{\cdot}8$.

It is evident that only at high mole ratios of phosphate to aluminium in solution (Table 1*b*) do the values of $q$ found correspond to the sorption of monomeric complexes such as $AlHPO_4^+$, $AlH_2PO_4^{2+}$, or $Al(H_2PO_4)_2^+$. Otherwise, over the ranges of mole ratios (Table 1*b*) and of pH values (Table 1*c*) studied the sorption of binuclear (or possibly polynuclear) complexes, similar to those found in the case of the ferric phosphate complexes,[9] is indicated. The values of $pN_{Al} - qN_{phosphate}$ shown in the last lines of Tables 1*b* and 1*c* have been derived by using the calculated values of $q$ for the respective complexes indicated. It can be seen that the agreement with the required value of unity is good. From the general similarity between the types of binuclear complexes sorbed by the exchanger in

[9] Holroyd and Salmon, *J.*, 1957, 959.
[10] Salmon, *Rev. Pure Appl. Chem.*, 1956, **6**, 24.

the two cases, it seems reasonable to suppose that $[Al_2(PO_4)OH)]^{2+}$ has the bridged structure $\left[Al\begin{matrix}<\\ \\ \end{matrix}\begin{matrix}PO_4\\ OH\end{matrix}\begin{matrix}>\\ \\ \end{matrix}Al\right]^{2+}$ analogous to that of the corresponding ferric phosphate complex.[9,11]

Bjerrum and Dahm [1] did not take into account, in their calculations, the possibility of the presence in solution of such binuclear phosphato-complexes. The difficulties which

TABLE 1. *Sorption of aluminium and phosphate by Zeo Karb* 225 (H-*form*, 0·500 *g.*) *from mixed solutions* (50 *ml.*) *of aluminium chloride and phosphoric acid or sodium dihydrogen phosphate.*

(*a*) $AlCl_3$ (0·1M), $H_3PO_4$ (0·33M); Al only sorbed.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Solution: | | | | | | | | | |
| Mole ratio $PO_4$ : Al | 0·00 | 0·21 | 0·40 | 0·72 | 1·03 | 1·40 | 1·84 | 3·02 | 4·90 |
| pH at equilibrium | 1·24 | 1·20 | 1·14 | 1·10 | 1·06 | 1·05 | 1·02 | 1·03 | 1·03 |
| Resin: | | | | | | | | | |
| $N_{Al}$ | 0·35 | 0·35 | 0·35 | 0·34 | 0·35 | 0·35 | 0·34 | 0·34 | 0·34 |
| $p$ | 2·86 | 2·86 | 2·86 | 2·94 | 2·86 | 2·86 | 2·94 | 2·94 | 2·94 |

(*b*) $AlCl_3$ (0·1M), $NaH_2PO_4$ (0·33M).

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Solution: | | | | | | | | |
| Mole ratio $PO_4$ : Al | 0·00 | 0·60 | 0·96 | 1·04 | 1·40 | 1·75 | 2·08 | 2·73 |
| pH at equilibrium | 1·36 | 1·41 | 1·47 | 1·45 | 1·52 | 1·60 | 1·71 | 1·82 |
| Resin: | | | | | | | | |
| $N_{Al}$ | 0·343 | 0·342 | 0·367 | 0·390 | 0·404 | 0·412 | 0·371 | 0·364 |
| $N_{phosphate}$ | — | 0·008 | 0·022 | 0·026 | 0·043 | 0·053 | 0·036 | 0·040 |
| $p$ | 2·92 | — | — | — | — | — | — | — |
| $q$ | — | — | 2·9 | 5·0 | 4·0 | 3·6 | 2·1 | 1·4 |
| Poss. complex * | — | — | a | c | b | b | d | e/f |
| $q$ for complex | — | — | 2·8 | 4·8 | 3·8 | 3·8 | 1·9 | 0·9/0·95 |
| $pN_{Al}$–$qN_{phosphate}$ | — | — | 1·00 | 1·01 | 1·01 | 0·99 | 1·01 | 1·02 |

(*c*) $AlCl_3$ (0·1M), $H_3PO_4$ (0·33M), $NaH_2PO_4$ (0·33M).

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Solution: | | | | | | | | |
| Mole ratio $PO_4$ : Al | 1·04 | → throughout | | | | | | |
| pH at equilibrium | 1·06 | 1·12 | 1·13 | 1·18 | 1·19 | 1·29 | 1·34 | 1·45 |
| Resin: | | | | | | | | |
| $N_{Al}$ | 0·340 | 0·345 | 0·360 | 0·370 | 0·370 | 0·370 | 0·380 | 0·390 |
| $N_{phosphate}$ | — | 0·005 | 0·012 | 0·015 | 0·019 | 0·019 | 0·020 | 0·026 |
| $p$ | 2·94 | — | — | — | — | — | — | — |
| $q$ | — | — | 3·7 | 4·8 | 3·8 | 3·8 | 5·1 | 5·0 |
| Poss. complex * | — | — | b | c | b | b | c | c |
| $q$ for complex | — | — | 3·8 | 4·8 | 3·8 | 3·8 | 4·8 | 4·8 |
| $pN_{Al}$–$qN_{phosphate}$ | — | — | 1·00 | 1·00 | 1·00 | 1·00 | 1·01 | 1·01 |

* a = $[Al_2(PO_4)]^{3+}$; b = $[Al_2(PO_4)(OH)]^{2+}$; c = $[Al_2(PO_4)(OH)_2]^{+}$; d = $[AlHPO_4]^{+}$; e = $[AlH_2PO_4]^{2+}$; f = $[Al(H_2PO_4)]_2^{+}$; and $N_{Al}$ and $N_{phosphate}$ are the moles of aluminium and phosphate respectively sorbed per equivalent of resin.

they encountered might well be due to this fact, for the present studies indicate that these bridged complexes may even be the predominant species in solution.

The results of the anion-exchange studies of the aluminium chloride–phosphate system (Table 2) are very similar to those obtained in studies of the ferric chloride–phosphate system.[6] In both systems no sorbable anionic complexes appear to be formed, even at high molar ratios of phosphate to metal (Table 2, *a*, *b*, and ref. 6). A twenty-fold increase in the concentrations of solutions (Table 2*c*) produced a slight degree of sorption only. There is evidently little tendency for chloro-complexes to be formed, as was indicated by Jensen.[2]

[11] Holroyd, Jameson, Odell, and Salmon, *J.*, 1957, 3239.

The amounts of aluminium and of zinc removed from the cation-exchanger Zeo-Karb 225 by the various acids, which are shown in Fig. 1, indicate the tendency for the reaction

$$\overline{M^{m+}} + mH^+ \rightleftharpoons M^{m+} + \overline{mH^+} \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

to proceed from left to right. Any complex formation in solution will lower the effective concentration of $M^{m+}$ and hence will drive the reaction from left to right. Hence for

TABLE 2. *Sorption of chloride, phosphate, and aluminium by* I.R.A.-400 (Cl-*form*, 1·000 *g.*) *from mixed solutions* (*total* 50 *ml.*) *of aluminium chloride and phosphoric acid or sodium dihydrogen phosphate.*

(*a*) $AlCl_3$ (0·1M), $H_3PO_4$ (0·33M); Cl and $PO_4$ only sorbed.

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Solution: | | | | | | | | |
| Mole ratio $PO_4$ : Al ..... | 0 | 0·28 | 0·62 | 1·03 | 1·84 | 3·02 | 4·90 | 8·40 |
| pH at equilibrium ..... | 1·66 | 1·45 | 1·34 | 1·25 | 1·16 | 1·15 | 1·16 | 1·16 |
| Resin: | | | | | | | | |
| $N_{Cl}$ ..... | 1·00 | 1·00 | 0·97 | 0·95 | 0·97 | 0·94 | 0·91 | 0·86 |
| $N_{phosphate}$ ..... | — | 0·00 | 0·00 | 0·003 | 0·023 | 0·034 | 0·053 | 0·086 |

(*b*) $AlCl_3$ (0·1M), $NaH_2PO_4$ (0·33M); Cl and $PO_4$ only sorbed.

| | | |
|---|---|---|
| Solution: | | |
| Mole ratio $PO_4$ : Al ..... | 0·82 | 2·17 |
| Resin: | | |
| $N_{Cl}$ ..... | 0·98 | 0·94 |
| $N_{phosphate}$ ..... | 0·007 | 0·029 |

(*c*) $AlCl_3$ (2M), $H_3PO_4$ (2M).

| | | |
|---|---|---|
| Solution: | | |
| Mole ratio $PO_4$ : Al ..... | 0 | 1·00 |
| pH at equilibrium ..... | 0·25 | 0·12 |
| Resin: | | |
| $N_{Cl}$ ..... | 0·99 | 0·91 * |
| $N_{phosphate}$ ..... | — | 0·053 * |
| $N_{Al}$ ..... | — | 0·024 * |

* I.R.A.-400 used in the phosphate form. $N_{Al}$, $N_{Cl}$, and $N_{phosphate}$ represent the moles of aluminium, chloride, and phosphate respectively sorbed per equivalent of resin.

each metal the lowest curve must represent the closest approach to the simple equilibrium of equation 3, with a minimum disturbance from complex formation in solution, whilst the higher curves must correspond to an increasing degree of complex formation. As already indicated,[7] measurements made at the same pH values correspond to the same concentrations of $H_2PO_4^-$, $Cl^-$, and $ClO_4^-$ ions for phosphoric, hydrochloric, and perchloric acid—although the total phosphate concentration is high this is present mainly as undissociated phosphoric acid. Hence with aluminium there is evidently a decreasing tendency to complex formation in the order phosphate > chloride > perchlorate, but with zinc it decreases in the order chloride > phosphate > perchlorate. The marked extent of complex formation between aluminium and phosphate can be seen from a comparison of the data in Figs. 1*a* and*b*, which shows that while zinc is removed from the resin phase by solutions of a given pH more easily than is aluminium in the cases of hydrochloric and perchloric acid (*i.e.*, the ion of higher charge shows the greater affinity for the resin), the reverse is true in the case of phosphoric acid.

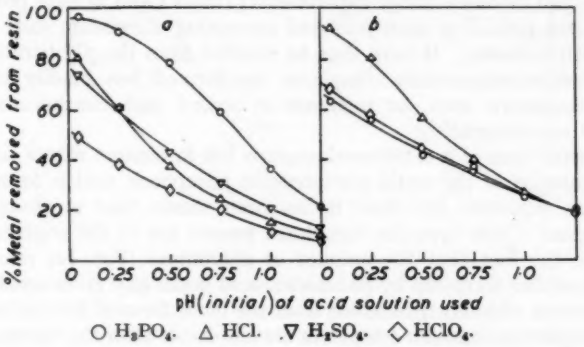
It is more difficult to assess the position in the " complexing series " of sulphuric acid since it will behave in part at least as a dibasic acid (cf. phosphoric acid which in this pH range is effectively monobasic), but in the pH range 0·50—1·25 sulphate appears to form stronger complexes with aluminium than does chloride. This conclusion is borne out by a consideration of the pH-titration results (Fig. 2) from which it is evident that in this pH

range the presence of sulphate adversely affects the release of hydrogen ions by reactions such as:

$$2Al^{3+} + H_3PO_4 \rightleftharpoons Al_2PO_4^{3+} + 3H^+ \quad . \quad . \quad . \quad . \quad . \quad (4)$$

This effect, which is markedly dependent on the amount of sulphate present, indicates that the sulphate ion forms complexes with aluminium which approach in stability those

FIG. 1. *Removal of* (*a*) $Al^{3+}$ *and* (*b*) $Zn^{2+}$ *from Zeo-Karb 225 by various acids.*



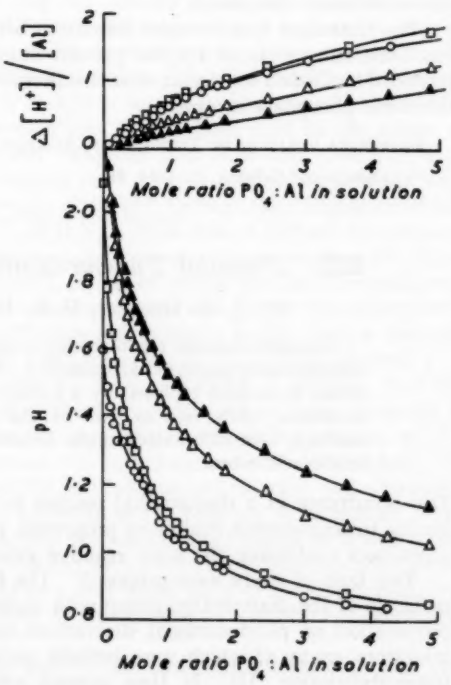




FIG. 2. *Titration of aluminium salt solutions* (0·1M *in* Al) *with phosphoric acid.*

○ $AlCl_3$.
△ $Al_2(SO_4)_3$.
▲ $Al_2(SO_4)_3 + (NH_4)_2SO_4$.
□ $Al(NO_3)_3$.

formed by the phosphate ion. Hence competitive complex formation by sulphate will limit the left-to-right reaction of equation 4 (for example), while sulphato-complexes present in the solution may exert a buffering effect:

$$AlSO_4^+ + H^+ \rightleftharpoons AlHSO_4^{2+} \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

XUM

The formation of chloro-complexes of aluminium appears to be slight at pH values above 0·75 (Fig. 1*a*) and in fact the pH-titration curve for aluminium chloride with phosphoric acid follows a very similar course to that for aluminium nitrate (Fig. 2).

A comparison of the pH-titration curve of any given aluminium salt (*e.g.*, nitrate, Fig. 2) with that of the corresponding ferric salt [4,6] shows that at any stage in the addition of the phosphoric acid the release of hydrogen ions is always less with the aluminium salt—except in the case of sulphate solutions at high mole ratios of phosphate to metal. Now the cation- and anion-exchange experiments (Tables 1 and 2) have provided evidence that the complexes formed in such solutions containing aluminium salts and phosphate are predominantly cationic. It may thus be inferred from the pH titration results that the cationic phosphatoaluminium complexes are formed less readily than the corresponding phosphatoferric ones, an inference in accord with conclusions based on the cation-exchange experiments.

When the metal form of a cation-exchanger is left in contact with a solution of phosphoric acid, a solution of the metal phosphate in phosphoric acid is formed by the ion-exchange process (equation 3). Now it has been shown that in aluminium or ferric phosphate solutions of this type the complexes formed are of the triphosphato (anionic) type.[3,12] Hence the fact that the amount of aluminium (Fig. 1*a*) removed from the aluminium form of Zeo-Karb 225 by phosphoric acid under any given conditions is always less than the amount of iron(III) removed from the ferric form of the exchanger [7] suggests that anionic phosphatoaluminium complexes are less stable than the corresponding anionic phosphatoferric complexes.

The statement that complex formation between aluminium and phosphate is marked [4] has been substantiated by the present studies. At the same time support has been provided for Dede's conclusion that the aluminium phosphate complexes are less stable than the ferric phosphate complexes.[5]

BATTERSEA COLLEGE OF TECHNOLOGY, LONDON, S.W.11. [*Received, October 21st,* 1957.]

[12] Jameson and Salmon, *J.*, 1954, 28.

---

## 222. *Potential Tumour-inhibitors based on Diazomethane.*

By J. A. HENDRY, F. L. ROSE, and A. L. WALPOLE.

Cyanuric chloride reacts readily in the cold with diazomethane to yield the corresponding dichlorodiazomethyl-1 : 3 : 5-triazine. The remaining chlorine atoms have been replaced by a variety of amine residues,* including ethyleneimine. Only one or two of the products exhibit tumour-inhibitory activity. An alternative route involved condensation of diguanides with oxalic acid esters.

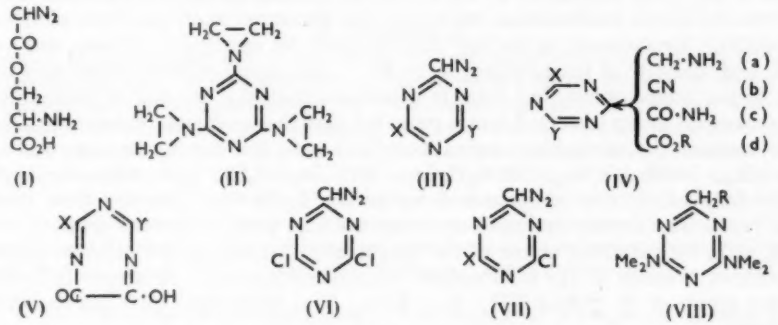
THE occurrence of a diazomethyl residue in "azaserine" [1] (I), an antibiotic substance having tumour-growth inhibitory properties, prompted the synthesis of a number of other substances containing the same reactive grouping for evaluation as anti-tumour agents.

Two lines of study were proposed. The first envisaged combination within the same molecule of the diazomethyl group with various amino-acid residues, and the second the preparation of polyfunctional derivatives analogous with the polyalkylating tumour-inhibitors, many of which were initially prepared in these laboratories, typified by the triaziridyltriazine (II). It then seemed evident that the simplest way in which to accomplish the first objective would be to employ the 1 : 3 : 5-triazine ring to provide also the conjunctive group linking the diazomethyl and amino-acid residues. For both

* Cf. B.P. 769,722.

[1] Stock, Reilly, Buckley, Clarke, and Rhoads, *Nature*, 1954, **173**, 71.

purposes, general methods were developed for the preparation of diazomethyl-1 : 3 : 5-triazines of type (III). While this work was being written up for publication, the synthesis of certain compounds related to (III) was described by Grundmann and Kober,[2] but in only one or two instances have the same compounds been prepared.




It was reasonable to suppose that the diazomethyl group in the triazines (III) would be comparatively unstable, and for this reason the first methods investigated aimed at the introduction of the X and Y substituents at early stages of the syntheses, leaving the diazomethyl group to be formed in the final step, for example by the action of nitrous acid on the corresponding aminomethyltriazine (IVa) or a derivative thereof such as the urea or toluene-*p*-sulphonamide. The most direct route to compounds (IV) appeared to be through the nitriles (IVb), formed in turn from the amides (IVc) and triazine esters (IVd). Since it was initially intended that X and Y should be amino-groups, the esters would be derived from oxalguanamines. Some attention has already been paid to the action of oxalic esters on diguanides. Overberger and Shapiro,[3] and Ridi and Checchi,[4] have shown that phenyldiguanide and diethyl oxalate react in cold methanolic solution with the rapid formation, not of the expected triazine ester, but, through the elimination of two molecules of ethanol, of a yellow product $C_{10}H_9O_2N_5$. Both sets of authors speculate on the structure of this substance which might contain the seven-membered ring (V; X = Ph·NH, Y = $NH_2$) (a triazatropolone structure), or one of several possible five-membered cyclic systems. We have effected similar condensations with $N^1$-*p*-chlorophenyl-$N^5$-dimethyldiguanide and $N^1N^1N^5$-trimethyl-$N^5$-phenyldiguanide. In the former instance the sparingly soluble colourless product gave analyses as for (V; X = *p*-Cl·$C_6H_4$·NH, Y = $NMe_2$), while the latter formed the triazine ester (IVd; X = NPhMe, Y = $NMe_2$, R = Et) freely soluble in organic solvents. Contact of these products with aqueous ammonia in dimethylformamide and methanol, respectively, gave the corresponding triazine amides (IVc), or alternatively from the former compound an isomer such as that derived from (V). These substances in turn gave the nitriles (IVb) with phosphoryl chloride, and ultimately the aminomethyltriazines by reduction with hydrogen in the presence of palladium. The conversion of the aminomethyl derivatives into the diazomethyl compounds was under investigation when the much simpler route starting with cyanuric chloride was discovered, and proceeded no further than the isolation of a very small yield of the compound (III; X = *p*-Cl·$C_6H_4$·NH, Y = $NMe_2$) by the action of nitrous acid in a mixture of acetic acid and benzene.

The alternative route followed from the observation that cyanuric chloride with two molecular proportions of diazomethane in ether gave the primary condensation product (VI) in good yield, the second molecule of diazomethane acting as an acid-binding agent

[2] Grundmann and Kober, *J. Amer. Chem. Soc.*, 1957, **79**, 944.
[3] Overberger and Shapiro, *ibid.*, 1954, **76**, 93.
[4] Ridi and Checchi, *Ann. Chim.* (*Italy*), 1953, **43**, 807.

giving nitrogen and (presumably) methyl chloride in the manner demonstrated by Bradley and Robinson [5] for the reaction of this substance with benzoyl chloride. The remaining chloride atoms in this product (VI) retained their reactivity and were replaced in subsequent experiments either with the same, or serially with different, substituents. For this purpose it was more convenient to use a benzene solution obtained after removal of the ether from the initial condensation, which step also discarded small quantities of unwanted by-products. Replacement of the first chlorine atom, for example by amines, was usually smooth and complete at temperatures up to 30°. The second chlorine substituent needed rather higher temperatures, but even in conditions requiring the use of boiling ethanol the diazomethyl group remained intact provided that the environment was kept alkaline. In this manner, the monochloro-derivatives (VII) were first made carrying substituents (X) = $NH_2$, NHMe, $NMe_2$, $NH{\cdot}C_6H_4Cl$-*p*, $NH{\cdot}CH_2{\cdot}CO_2Et$, and $NH{\cdot}C_6H_4{\cdot}CO_2Na$-*o*), and the fully substituted compounds listed in the Table were prepared from them by further reaction as already indicated or, where the final product was the symmetrical one with X = Y, by the direct action of the appropriate reagents on the dichloro-compound (VI) without isolation of the intermediate monochlorotriazines. Attempts to hydrolyse the ester group of compound (III; X = $NMe_2$, Y = $NH{\cdot}CH_2{\cdot}CO_2Et$) led to extensive breakdown.

| | Compound (III) | | Significant inhibition of: * | |
|---|---|---|---|---|
| Code no. | X | Y | Walker tumour | sarcoma 180 |
| 19,530 | $NH_2$ | $NMe_2$ | − | − |
| 19,911 | $NH_2$ | $NEt_2$ | − | − |
| 19,395 | NHMe | $NMe_2$ | ± | Nt |
| 18,488 | NHMe | $NH{\cdot}[CH_2]_2{\cdot}NEt_2$ | ± | Nt |
| 18,937 | $NMe_2$ | $NMe_2$ | + | + |
| 20,522 | $NMe_2$ | $NH{\cdot}CH_2{\cdot}CO_2Et$ | − | Nt |
| 21,274 | Morpholino | Morpholino | ± | − |
| 21,275 | $N<C_5H_{10}$ | $N<C_5H_{10}$ | − | − |
| 18,584 | $NH{\cdot}[CH_2]_2{\cdot}NEt_2$ | $NH{\cdot}C_6H_4Cl$-*p* | − | − |
| 19,190 | $N<[CH_2]_5$ | $N<[CH_2]_5$ | + | + |
| 18,394 | NHMe | Cl | − | − |
| 18,936 | $NH{\cdot}C_6H_4Cl$-*p* | Cl | − | − |
| 20,290 | $NH{\cdot}CH_2{\cdot}CO_2Et$ | Cl | − | − |

* Compounds in which X = $NH_2$, Y = $NH{\cdot}[CH_2]_2{\cdot}NEt_2$, OMe, and SEt, and (no. 19,394) X = $NMe_2$, Y = $NH{\cdot}C_6H_4Cl$-*p*, were not subjected to either test. Nt = not tested.

All of the above triazines carrying the diazomethyl group were sensitive to acids, decomposing with vigorous evolution of nitrogen. The chemical nature of the decomposition products was examined in some detail in the case of compound (III; X = Y = $NMe_2$). After decomposition in hot dilute sulphuric acid, the hydroxymethyltriazine (VIII; R = OH) was finally isolated, but the alkali-solubility of the reaction product at the earlier stages of the decomposition suggested that the sulphuric ester might have been an intermediate. Hot dilute hydrochloric acid gave a high yield of the chloromethyl product (VIII; R = Cl), while cold glacial acetic acid formed the acetoxy-derivative (VIII; R = OAc). Similarly, 3 : 4 : 5-trimethoxybenzoic acid in boiling benzene gave the acyloxymethyltriazine, and the same reaction effected in boiling methanol gave the methoxymethyltriazine as a by-product in substantial amount.

Most of the compounds have been examined for inhibitory action upon the growth of the Walker carcinoma 256 in rats, or the Crocker sarcoma 180 in mice, or both. With the Walker tumour the procedure adopted was essentially similar to that already described.[6] With sarcoma 180 the method used was a modification of that described by Stock.[7] Several of the compounds, given by daily intraperitoneal injection in maximal sub-lethal doses to tumour-bearing rats, caused a marked fall in the gross weight of the tumour-bearing animals. Only two inhibited tumour-growth to an extent which was clearly greater than could be accounted for by their general "toxic" effect, indicated by the

[5] Bradley and Robinson, *J.*, 1928, 1310.
[6] Walpole, *Brit. J. Pharmacol.*, 1951, **6**, 135; Hendry, Rose, and Walpole, *ibid.*, p. 201.
[7] Stock, *Amer. J. Med.*, 1950, **8**, 658.

fall in gross weight referred to. The activity of one of these (18,937) recalls that of tris(dimethylamino)triazine,[8] than which it is in fact more active. Further tests however, showed that 18,937 is almost inactive when given by mouth and unsuitable for parenteral administration in man. The other active compound (19,190) is inferior in activity to other polyfunctional ethyleneimines.

## Experimental

*Reaction of Diguanides with Oxalic Esters.*—(a) $N^1$-p-*Chlorophenyl*-$N^5$-*dimethyldiguanide.* Dimethyl oxalate (22 g.) in methanol (50 c.c.) was added to a stirred solution of the diguanide (25 g.) in methanol (400 c.c.) initially at 30°. The heavy crystalline deposit that was rapidly formed was collected, washed with methanol, and used without further purification for conversion into the amide (below). A specimen of the *product* crystallised from dimethylformamide in colourless needles, m. p. 310° (decomp.) (Found: C, 48·7; H, 4·3; N, 22·9. $C_{12}H_{12}O_2N_5Cl$ requires C, 49·05; H, 4·1; N, 23·85. The triazine ester requires C, 50·74; H, 4·55; N, 22·75%).

(b) $N^1$-*Phenyldiguanide.* Similarly prepared from the diguanide (20 g.) and dimethyl oxalate (20 g.), the reaction mixture being set aside for 2 hr., the *product* formed pale yellow leaflets [19·2 g.; m. p. 218° (decomp.)]. Overberger and Shapiro [9] give m. p. 222—225° (decomp.).

(c) $N^1N^1N^5$-*Trimethyl*-$N^5$-*phenyldiguanide.* The diguanide (5·5 g.) and diethyl oxalate (4·4 g.) were heated together on the steam-bath for 1 hr., after which the excess of ester was removed under reduced pressure. The residual oily *product* (Found: C, 59·4; H, 6·8; N, 24·3. $C_{15}H_{19}O_2N_5$ requires C, 59·8; H, 6·3; N, 23·3%) was freely soluble in organic solvents, but attempts to isolate it by distillation led to decomposition. It was used directly for conversion into the amide.

2-*Carbamoyl*-4-p-*chloroanilino*-6-*dimethylamino*-1 : 3 : 5-*triazine.*—The crude moist product from (a) above was shaken for 20 hr. with aqueous ammonia (200 c.c.; *d* 0·88) and dimethylformamide (100 c.c.). The colourless *amide* that resulted (18 g.; m. p. 289—291°) was filtered off. If formed colourless prisms (from dimethylformamide), m. p. 301—302° (Found: C, 49·2; H, 4·8; N, 29·0. $C_{12}H_{13}ON_6Cl$ requires C, 49·2; H, 4·4; N, 28·7%).

2-p-*Chloroanilino*-4-*cyano*-6-*dimethylamino*-1 : 3 : 5-*triazine.*—The clear solution formed when the above crude amide (150 g.) and phosphoryl chloride (700 c.c.) were refluxed for 3 hr. was distilled under reduced pressure to remove excess of the latter (400 c.c.) and then decomposed in ice-water. The *nitrile* (93 g.; m. p. 198—200°) was obtained sensibly pure by lixiviation in water (5 l.) at 40° and crystallisation (charcoal) from acetic acid. It formed colourless needles (from toluene), m. p. 200° (Found: C, 52·5; H, 4·1; N, 31·0; Cl, 13·3. $C_{12}H_{11}N_6Cl$ requires C, 52·5; H, 4·0; N, 30·6; Cl, 12·9%).

2-*Aminomethyl*-4-p-*chloroanilino*-6-*dimethylamino*-1 : 3 : 5-*triazine.*—The above nitrile (14 g.), suspended in methanol (125 c.c.) and concentrated hydrochloric acid (5 c.c.), was reduced with hydrogen at room temperature and pressure over palladium chloride (0·2 g.). The methanolic filtrate after removal of the catalyst was evaporated to dryness, the residue digested in boiling 0·25N-hydrochloric acid (300 c.c.) (charcoal) and filtered, and concentrated hydrochloric acid (100 c.c.) added. The *dihydrochloride* crystallised in colourless needles, m. p. 298° (decomp.) (Found: C, 39·8; H, 5·0; N, 23·3; Cl, 19·7. $C_{12}H_{15}N_6Cl,2HCl,\frac{1}{2}H_2O$ requires C, 39·9; H, 5·0; N, 23·3; Cl, 19·6%).

2-p-*Chloroanilino*-4-*diazomethyl*-6-*dimethylamino*-1 : 3 : 5-*triazine.*—Sodium nitrite (0·5 g.) was added to a mixture of the above aminomethyltriazine (0·5 g. of base, prepared by the addition of sodium hydroxide to an aqueous solution of the dihydrochloride), glacial acetic acid (5 c.c.), and benzene (5 c.c.) and shaken for 5 min. at 10—20°. Water was added and the yellow benzene layer was washed with dilute aqueous sodium carbonate and water and dried ($K_2CO_3$). The solution was applied to an alumina column and eluted with 1 : 19 methanol–benzene. The light yellow band was collected in an eluate which was evaporated. The residue was digested with light petroleum (b. p. 80—100°) and filtered. The solid left after evaporation of the petroleum recrystallised from methanol, affording the bright yellow *diazomethyl derivative* (20 mg.), m. p. 153°; mixed m. p. with material prepared as described below, 142—153°.

Treatment of a solution at 50° of the aminomethyltriazine in dilute hydrochloric acid with

[8] Buckley, Stock, Crossley, and Rhoads, *Cancer Res.*, 1950, **10**, 208; Hendry, Homer, Rose, and Walpole, *Brit. J. Pharmacol.*, 1951, **6**, 357.

sodium nitrite gave a colourless crystalline precipitate of the hydrochloride of 2-p-*chloroanilino*-4-*dimethylamino*-6-*hydroxymethyl*-1 : 3 : 5-*triazine* which was shaken with dilute sodium carbonate and extracted by ethyl acetate, recovered, and recrystallised from toluene, affording colourless prisms, m. p. 183—184° (Found: C, 51·0; H, 4·9; N, 24·1. $C_{12}H_{14}ON_5Cl$ requires C, 51·5; H, 5·0; N, 24·9%).

2-*Carbamoyl*-4-*dimethylamino*-6-N-*methylanilino*-1 : 3 : 5-*triazine*.—The oily ester from (c) above was shaken in methanol (10 c.c.) for 2 hr. with aqueous ammonia (50 c.c.; *d* 0·88). The precipitate of crude *amide* (2·85 g.; m. p. 112°) afforded colourless rosettes (from benzene), m. p. 125° (Found: C, 57·6; H, 6·1; N, 30·3. $C_{13}H_{16}ON_6$ requires C, 57·3; H, 5·9; N, 30·8%).

2-*Cyano*-4-*dimethylamino*-6-N-*methylanilino*-1 : 3 : 5-*triazine*, prepared as described above from the amide (6·7 g.) and phosphoryl chloride (30 c.c.), afforded colourless needles (3·7 g.), m. p. 120°, from light petroleum (b. p. 100—120°) (Found: C, 61·3; H, 5·8; N, 33·5. $C_{13}H_{14}N_6$ requires C, 61·4; H, 5·5; N, 33·1%).

Reduction of the nitrile (1·4 g.) in methanol (50 c.c.) containing concentrated hydrochloric acid (0·55 c.c.) with hydrogen (240 c.c.; theor. 246 c.c.) over palladium chloride (0·1 g.), filtration and evaporation to small bulk gave colourless 2-*aminomethyl*-4-*dimethylamino*-6-N-*methylanilino*-1 : 3 : 5-*triazine hydrochloride*, m. p. 252—253° (Found: C, 49·9; H, 6·7; N, 26·8; Cl, 16·6. $C_{13}H_{18}N_6.1\frac{1}{2}HCl$ requires C, 49·9; H, 6·2; N, 26·9; Cl, 17·0%).

*Preparations involving the Use of Diazomethane.* (a) *Intermediates.*—2 : 4-*Dichloro*-6-*diazomethyl*-1 : 3 : 5-*triazine*. Cyanuric chloride (25 g.) was added during 25 min. to a stirred solution of diazomethane (13·3 g.) in ether (700 c.c.) at 7—10°. Evolution of nitrogen was complete after 1 hr., then the solvent was removed under reduced pressure. The residue was dissolved in benzene (170 c.c.) and the solution, after being dried ($CaCl_2$) and clarified with charcoal, was used without further treatment in the preparations described immediately below. The solid left by removal of the solvent from a small volume of the solution afforded the dichlorodiazomethyltriazine as yellow needles [from light petroleum (b. p. 60—80°)], m. p. 115—118° (Found: C, 25·5; H, 0·5; N, 36·1; Cl, 37·3. Calc. for $C_4HN_5Cl_2$: C, 25·25; H, 0·5; N, 36·8%; Cl, 37·35%). Grundmann and Kober [2] give m. p. 111·5—112·5°.

2-*Amino*-4-*chloro*-6-*diazomethyl*-1 : 3 : 5-*triazine*. A benzene solution of dichlorodiazomethyltriazine (prepared as above from 31·8 g. of cyanuric chloride) was added during 10 min. to a stirred mixture of concentrated aqueous ammonia (88 c.c.) and water (88 c.c.) kept at 10—15°. After 1¼ hr. the crude aminotriazine [33 g.; m. p. 168° (decomp.)] was filtered off, washed with water, dried, and used without further purification in subsequent preparations. A small sample gave pale yellow crystals, m. p. 180—181° (decomp.), from much benzene (Found: C, 28·5; H, 2·2; N, 47·8. Calc. for $C_4H_3N_6Cl$: C, 28·15; H, 1·75; N, 49·2%). Grundmann and Kober [2] give m. p. 186° (decomp.).

2-*Chloro*-4-*diazomethyl*-6-*methylamino*-1 : 3 : 5-*triazine*. 30% Aqueous methylamine (30 c.c.) was added slowly to a stirred solution of the above dichlorodiazomethyltriazine (from 9·2 g. of cyanuric chloride) in benzene at <40°. The crude precipitated *methylaminotriazine* (6 g.; (decomp. 190°) recrystallised from dimethylformamide as pale yellow plates, decomp. 210° (Found: C, 32·8; H, 3·0; N, 44·4; Cl, 20·3. $C_5H_5N_6Cl$ requires C, 32·5; H, 2·7; N, 45·5; Cl, 19·25%).

2-*Chloro*-4-*diazomethyl*-6-*dimethylamino*-1 : 3 : 5-*triazine*. This was similarly prepared from the dichlorodiazomethyltriazine (from 10 g. of cyanuric chloride) and 29·4% aqueous dimethylamine (20 c.c.) at 5—10°. The benzene layer was dried ($CaCl_2$) and the solvent removed below 40°. The residue, recrystallised from light petroleum, then ethanol, gave the pale yellow *dimethylaminotriazine*, m. p. 102—103° (Found: C, 36·3; H, 3·6; N, 39·3; Cl, 18·3. $C_6H_7N_6Cl$ requires C, 36·25; H, 3·5; N, 42·3; Cl, 17·9%).

2-*Chloro*-4-p-*chloroanilino*-6-*diazomethyl*-1 : 3 : 5-*triazine*. A solution of *p*-chloroaniline (7·05 g.) in benzene (45 c.c.) was stirred in a mixture of the dichlorodiazomethyltriazine (from 9 g. of cyanuric chloride) in benzene, and potassium carbonate (13·8 g.) in water (90 c.c.) for 2 hr. at 35—40°. The crude p-*chloroanilinotriazine* [8·4 g.; m. p. 188° (decomp.)] obtained on filtration was sufficiently pure for further use, but a little, recrystallised from methanol, gave pale yellow needles, m. p. 193° (Found: C, 43·0; H, 1·8. $C_{10}H_6N_6Cl_2$ requires C, 42·7; H, 2·1%).

2-o-*Carboxyanilino*-4-*chloro*-6-*diazomethyl*-1 : 3 : 5-*triazine*. Similarly prepared from reaction of a solution of anthranilic acid (10 g.) in water (110 c.c.) and anhydrous sodium carbonate (15 g.), with the dichlorodiazomethyltriazine in benzene (from 9·2 g. of cyanuric chloride), this was isolated as the *sodium salt* by filtration and washing with 20% aqueous sodium

acetate. The salt was purified (7·5 g.; pale yellow prisms) by reprecipitation from water (580 c.c.) with sodium acetate (250 g.), followed by crystallisation (charcoal) from methanol (250 c.c.) and water (sufficient to dissolve at the boil) (Found, after drying at 100°: C, 38·5; H, 2·8; N, 23·8; Cl, 10·9. $C_{11}H_8O_2N_6ClNa,2H_2O$ requires C, 37·9; H, 2·85; N, 24·1; Cl, 10·8%).

*2-Chloro-4-diazomethyl-6-ethoxycarbonylmethylamino-1 : 3 : 5-triazine.* Dichlorodiazomethyltriazine in benzene (from 22·4 g. of cyanuric chloride) was added during 10 min. to a stirred solution of glycine ethyl ester hydrochloride in N-sodium hydroxide (300 c.c.). After 2 hours' stirring at 35—40° the suspension was cooled to 10° and filtered. Recrystallisation of the crude *ester* (17·6 g.) from methanol gave pale yellow crystals, m. p. 153° (decomp.) (Found: C, 37·7; H, 3·1; N, 30·5. $C_8H_8O_2N_6Cl$ requires C, 37·4; H, 3·5; N, 32·75%).

(b) *Final Products containing Diazomethyl Residues.*—*2-Amino-4-diazomethyl-6-dimethylamino-1 : 3 : 5-triazine.* 2-Amino-4-chloro-6-diazomethyl-1 : 3 : 5-triazine (1 g.) was stirred in 20% aqueous dimethylamine (5 c.c.) for 15 min. at 40—45°. The crude *product* (m. p. 150°) gave pale yellow crystals, m. p. 152° (decomp.), from methanol (Found: C, 40·7; H, 5·5; N, 54·6. $C_6H_9N_7$ requires C, 40·2; H, 5·0; N, 54·7%).

*2-Amino-4-diazomethyl-6-diethylamino-1 : 3 : 5-triazine.* Similarly prepared from 2-amino-4-chloro-6-diazomethyl-1 : 3 : 5-triazine (11 g.), diethylamine (30 c.c.), and water (30 c.c.), the crude *product* had m. p. 137—140° and, after recrystallisation from ethanol, m. p. 146—148° (Found: C, 46·4; H, 6·7; N, 46·9. $C_8H_{13}N_7$ requires C, 46·35; H, 6·3; N, 47·35%).

*2-Amino-4-diazomethyl-6-3′-(diethylamino)propylamino-1 : 3 : 5-triazine.* 2-Amino-4-chloro-6-diazomethyl-1 : 3 : 5-triazine (1 g.) and diethylaminopropylamine (2 g.) were mixed and kept at 60—65° for 10 min. The solution obtained by adding water was extracted twice with benzene, and the benzene layer washed with water, dried ($Na_2SO_4$), and applied to an alumina column. Concentration of the eluate (1 : 49 methanol–benzene) gave a pale yellow *product*, m. p. 106—108° (Found: C, 50·1; H, 7·4; N, 42·1. $C_{11}H_{20}N_8$ requires C, 50·0; H, 7·6; N, 42·4%).

*2-Amino-4-diazomethyl-6-methoxy-1 : 3 : 5-triazine.* 2-Amino-4-chloro-6-diazomethyl-1 : 3 : 5-triazine (1·7 g.) and methanol (25 c.c.), in which sodium (0·46 g.) had previously been dissolved, were refluxed for 15 min. The cooled suspension was filtered, and the residue (m. p. 170°) left after evaporation of the filtrate crystallised from benzene. The *product* then had m. p. 182° (decomp.) (Found: C, 35·8; H, 3·9; N, 49·9. $C_5H_6ON_6$ requires C, 36·1; H, 3·6; N, 50·6%).

*2-Amino-4-diazomethyl-6-ethylthio-1 : 3 : 5-triazine.* A mixture of 2-amino-4-chloro-6-diazomethyl-1 : 3 : 5-triazine (1·7 g.), ethanethiol (1·5 c.c.), and methanol (25 c.c.), in which sodium (0·23 g.) had previously been dissolved, was refluxed for 15 min. The crude *product* obtained after cooling, filtration, and evaporation of the filtrate gave needles (from methanol), m. p. 204° (decomp.) (Found: C, 36·9; H, 5·3; N, 42·2; S, 15·6. $C_6H_8N_6S$ requires C, 36·75; H, 4·1; N, 42·85; S, 16·3%).

*2-Diazomethyl-4-dimethylamino-6-methylamino-1 : 3 : 5-triazine.* The above 2-chloro-4-diazomethyl-6-methylamino-1 : 3 : 5-triazine (9·2 g.) was stirred into 20% aqueous dimethylamine (45 c.c.) initially at 45°. A period of complete solution was followed rapidly by crystallisation of the *product* (7·2 g.), which had m. p. 118—120° when recrystallised from ethanol (Found: C, 43·9; H, 5·8; N, 48·8. $C_7H_{11}N_7$ requires C, 43·5; H, 5·7; N, 50·8%).

*2-Diazomethyl-4-diethylaminopropylamino-6-methylamino-1 : 3 : 5-triazine.* Prepared and purified as described above for 2-amino-4-diazomethyl-6-3′-(diethylamino)propylamino-1 : 3 : 5-triazine, from 2-chloro-4-diazomethyl-6-methylamino-1 : 3 : 5-triazine (6·6 g.) and diethylaminopropylamine (15 g.), the *product* (6 g.) had m. p. 50—51° (Found: C, 51·6; H, 8·1; N, 40·8. $C_{12}H_{22}N_8$ requires C, 51·8; H, 7·9; N, 40·3%).

*2 : 4-Diaziridyl-6-diazomethyl-1 : 3 : 5-triazine.* Dichlorodiazomethyltriazine (from 8·6 g. of cyanuric chloride) in benzene was added to a solution of ethyleneimine (6·9 g.) and triethylamine (16·5 g.) in benzene (50 c.c.) stirred at 10°. After 3 hr. the suspension was filtered and the filtrate evaporated under reduced pressure. The residue (7·2 g.) was continuously extracted with boiling light petroleum (b. p. 40—60°). The extracted product recrystallised from light petroleum–ethyl acetate as pale yellow felted prismatic needles, decomp. 120° without melting (Found: C, 47·5; H, 4·2; N, 48·0. Calc. for $C_8H_9N_7$: C, 47·3; H, 4·4; N, 48·3%). Grundmann and Kober [2] give decomp. 108° without melting.

*2-Diazomethyl-4 : 6-dimorpholino-1 : 3 : 5-triazine.* Dichlorodiazomethyltriazine (from 10·4 g. of cyanuric chloride) in benzene was added dropwise to morpholine (21·8 g.) and water

(60 c.c.) kept at 40°. After 2 hr. at 35—40°, the precipitate (9·4 g.) which was formed was collected, washed with water and benzene, and dried *in vacuo*. The *product* formed pale yellow microcrystals, m. p. 198°, from benzene (Found: C, 49·6; H, 5·8; N, 33·4. $C_{12}H_{17}O_2N_7$ requires C, 49·5; H, 5·85; N, 33·7%).

2-*Diazomethyl*-4 : 6-*dipiperidino*-1 : 3 : 5-*triazine*. Similarly prepared from the dichlorotriazine (from 10·4 g. of cyanuric chloride) in benzene, piperidine (21·2 g.), and water (60 c.c.), the *product* remained dissolved in the benzene layer and was obtained by separation and evaporation of the solvent, followed by recrystallisation from light petroleum (b. p. 80—100°); it had m. p. 107° (Found: C, 58·9; H, 6·9; N, 28·8. $C_{14}H_{21}N_7$ requires C, 58·5; H, 7·3; N, 34·1%).

2-*Diazomethyl*-4 : 6-*bisdimethylamino*-1 : 3 : 5-*triazine*. Similarly prepared from the dichlorotriazine (from 10·4 g. of cyanuric chloride) in benzene and 30% aqueous dimethylamine (37 g.), the *product* likewise remained dissolved in the benzene layer. It finally recrystallised from light petroleum (b. p. 80—100°) as yellow rosettes, m. p. 94° (Found: C, 46·2; H, 6·0; N, 47·3. $C_8H_{13}N_7$ requires C, 46·4; H, 6·3; N, 47·3%).

2-*Diazomethyl*-4-*dimethylamino*-6-*ethoxycarbonylmethylamino*-1 : 3 : 5-*triazine*. Powdered 2-chloro-4-diazomethyl-6-ethoxycarbonylmethylamino-1 : 3 : 5-triazine (10 g.) was stirred into 30% aqueous dimethylamine (50 c.c.) at 20°. The crystalline product (m. p. 129°) which was precipitated from the initially complete solution was collected and recrystallised from methanol; it had m. p. 138° (Found: C, 44·7; H, 5·4; N, 36·3. $C_{10}H_{15}O_2N_7$ requires C, 45·2; H, 5·6; N, 37·0%).

2-p-*Chloroanilino*-4-*diazomethyl*-6-*dimethylamino*-1 : 3 : 5-*triazine*. Similarly prepared from 2-chloro-4-*p*-chlorophenylamino-6-diazomethyl-1 : 3 : 5-triazine (7·7 g.) and 30% aqueous dimethylamine (75 c.c.), the yellow *product*, m. p. 153°, recrystallised from methanol (Found: C, 49·8; H, 5·0; N, 34·3. $C_{12}H_{13}N_7Cl$ requires C, 49·75; H, 4·15; N, 33·85%).

2-p-*Chloroanilino*-4-*diazomethyl*-6-*diethylaminopropylamino*-1 : 3 : 5-*triazine*. Prepared and purified as described above for the corresponding 2-aminotriazine, from 2-chloro-4-*p*-chlorophenylamino-6-diazomethyl-1 : 3 : 5-triazine (1·7 g.) and diethylaminopropylamine (2 g.), the *product* formed a colourless crystalline powder, m. p. 86—87° (Found : C, 54·2; H, 5·8; N, 29·9; Cl, 9·7. $C_{17}H_{23}N_8Cl$ requires C, 54·45; H, 6·15; N, 29·9; Cl, 9·5%).

2 : 4-*Bisdimethylamino*-6-*hydroxymethyl*-1 : 3 : 5-*triazine and esters therefrom*. The above diazomethyl-bisdimethylaminotriazine (10 g.) was added portionwise to cooled 2N-sulphuric acid (50 c.c.) and stirred until evolution of nitrogen had ceased. The resultant solution was gently boiled for 10 min., basified while still hot with dilute aqueous sodium hydroxide, cooled to 55° (the slight precipitate being discarded), then kept at room temperature overnight. The *product* crystallised in pale cream rhombs, m. p. 67—68° (Found: C, 48·6; H, 7·1; N, 33·0. $C_8H_{16}ON_6$ requires C, 48·7; H, 7·6; N, 35·5%).

A similar decomposition (8 g.) in 2N-hydrochloric acid led to an immediate oily precipitate (6 g.) on hot basification which when recrystallised twice from methanol gave 2-*chloromethyl*-4 : 6-*bisdimethylamino*-1 : 3 : 5-*triazine*, m. p. 78—80° (Found: C, 44·9; H, 6·7; N, 32·2. $C_8H_{14}N_6Cl$ requires C, 44·6; H, 6·5; N, 32·5%). The hydroxymethyl derivative (0·75 g.; m. p. 67—68°) was recovered from the cooled aqueous mother-liquors.

2-*Acetoxymethyl*-4 : 6-*bisdimethylamino*-1 : 3 : 5-*triazine* (2·3 g.) was likewise obtained as colourless prismatic needles, m. p. 68—70° (Found: C, 49·9; H, 7·6; N, 28·0. $C_{10}H_{17}O_2N_5$ requires C, 50·2; H, 7·1; N, 29·3%), when water (50 c.c.) was added to the diazomethyltriazine (5 g.) in cooled glacial acetic acid (10 c.c.).

2 : 4-*Bisdimethylamino*-6-(3 : 4 : 5-*trimethoxybenzoyloxymethyl*)-1 : 3 : 5-*triazine*, colourless plates (2·5 g.), m. p. 129—130° (Found: N, 17·8. $C_{18}H_{25}O_5N_5$ requires N, 17·9%), was obtained by recrystallisation from light petroleum (b. p. 80—100°) of the product from the diazomethyltriazine (2·4 g.) and 3 : 4 : 5-trimethoxybenzoic acid (3·1 g.) in dry refluxing benzene (50 c.c.) (2 hr.). An attempt to effect the same reaction in methanol gave 30% of a by-product, 2 : 4-*bisdimethylamino*-6-*methoxymethyl*-1 : 3 : 5-*triazine*, m. p. 49—51°, separated by dissolution in dilute hydrochloric acid and reprecipitation with sodium hydroxide, and recrystallised from light petroleum (b. p. 40—60°) (Found: C, 51·3; H, 8·1; N, 33·7. $C_9H_{17}ON_5$ requires C, 51·2; H, 8·05; N, 33·2%).

Research Department,
Imperial Chemical Industries Limited, Pharmaceuticals Division,
Alderley Park, Macclesfield, Cheshire.
[*Received, October 15th*, 1957.]

## 223. *Acyl* iso*Thiocyanates. Part II.* Reactions of Aroyl* iso*Thiocyanates with Amines and Amino-acids in Aqueous Solution.*

By D. T. Elmore and J. R. Ogle.

Hydrolysis of benzoyl *iso*thiocyanate affords benzamide, dibenzoylamine, and benzoic acid in amounts which depend on pH; a mechanism is advanced to account for the observations. With amino-acids in aqueous dioxan at alkaline pH, benzoyl *iso*thiocyanate in general affords the *N*-benzoyl derivative. Addition may compete or even predominate if (i) the distance between the amino- and the carboxylate group is large (*e.g.*, as in 6-aminohexanoic acid), (ii) the amino-group is attached to an aromatic ring, or (iii) substitution is sterically hindered. 2 : 4 : 6-Tribromobenzoyl *iso*thiocyanate gives exclusively addition products.

In continuation of earlier work,[1] and as a variation of Edman's method [2] of stepwise degradation of peptides from the *N*-terminus, it was of interest to attempt the synthesis of *N*-acylthiocarbamoylamino-acids and -peptides by the interaction of acyl *iso*thiocyanates and amino-acids and peptides in aqueous solvents at alkaline pH. The observation that condensation between methyl *N*-acetyldithiocarbamate and some amino-acids and peptides proceeded slowly was an additional incentive. We have already indicated [3,4] that the reactions of acyl *iso*thiocyanates are complex, since addition to the ·N:C:S system and nucleophilic substitution at the carbonyl-carbon atom may compete with one another. The rates of these reactions depend on factors such as basic strength of nucleophilic reagent, solvent polarity, structure of acyl *iso*thiocyanate, and temperature. Since aroyl *iso*thiocyanates generally react additively (for exceptions see refs. 5, 6), we decided to examine the reactions between benzoyl *iso*thiocyanate and amino-acids in aqueous solvents.[3]

The mode of hydrolysis of benzoyl *iso*thiocyanate depends on pH. In water, benzamide was formed in over 80% yield, presumably through the intermediate thiocarbamic acid, together with a trace of benzoic acid, thus confirming earlier work.[6,7] On the other hand, Dixon and Taylor [6] found that N-sodium hydroxide liberated thiocyanate ion almost quantitatively. We have found that reaction of benzoyl *iso*thiocyanate in aqueous dioxan at pH 8·5 and pH 6·3, followed by acidification, affords a mixture of benzamide, dibenzoylamine, and benzoic acid (Table 1). Dibenzoylamine, which has not previously been reported

Table 1. *Hydrolysis of benzoyl* iso*thiocyanate.*

| Solvent | pH | Alkali uptake (mole/mole *iso*thiocyanate) | Yield (%) of mixed amides | Yield (%) of benzoic acid |
|---|---|---|---|---|
| Water–ether ..... | — | — | 81·5[a] | 3·0 |
| Water–ether (5 : 1) ..... | 6·3 | 0·45 | 73·5 | 34·4 |
| Water–dioxan (3 : 2) ..... | 8·5 | 1·20 | 52·8 | 43·8 |
| Water–dioxan (1 : 1) ..... | 8·5 | 1·02 | 51·2[b] | 47·9 |

[a] Pure benzamide. [b] Composed of benzamide 13·9% and dibenzoylamine 37·3%.

as a product of hydrolysis of benzoyl *iso*thiocyanate, presumably arises from nucleophilic attack by *N*-benzoylthiocarbamate ion (I) on benzoyl *iso*thiocyanate followed by loss of carbon oxysulphide from the resultant unsymmetrical acid anhydride (II). As expected, the yields of benzamide and dibenzoylamine were lower at the higher pH.

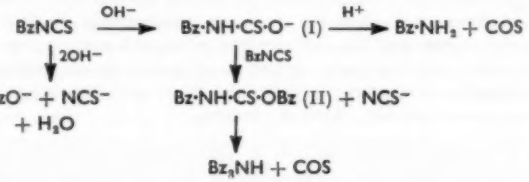
* Part I, *J.*, 1956, 4458.

[1] Elmore and Toseland, *J.*, 1954, 4533; 1957, 2460.
[2] Edman, *Acta Chem. Scand.*, 1950, **6**, 283.
[3] Elmore and Ogle, *Proc. Chem. Soc.*, 1957, 289.
[4] Elmore, Ogle, Fletcher, and Toseland, *J.*, 1956, 4558 and references cited therein.
[5] Wheeler, *Amer. Chem. J.*, 1901, **26**, 345; Hoggarth, *J.*, 1949, 1160.
[6] Dixon and Taylor, *J.*, 1908, **93**, 684.
[7] Miquel, *Ann. Chim.*, 1877, **10**, 289.



XUM

Although hydrolysis of benzoyl *iso*thiocyanate was quite fast, in general it did not seriously compete with the reactions involving amines, amino-acids, and peptides, and the combined yields of *N*-benzoyl and *N*-benzoylthiocarbamoyl derivatives usually accounted for more than 70% of the base used (Table 2). Notable exceptions were the reactions involving methylamine, γ-aminobutyric acid, 6-aminohexanoic acid, and 1-amino*cyclo*hexanecarboxylic acid. The high p$K_a$ values of the first three (10·64, 10·43, and 10·75 respectively at 25°) probably explain the low yields, since the small degree of dissociation would allow hydrolysis of *iso*thiocyanate to compete seriously. The p$K_a$ of 1-amino*cyclo*-




hexanecarboxylic acid has not been measured, but it is likely to be at least as high as that of α-amino*iso*butyric acid (10·21 at 25°). The uptake of alkali (Table 2) provides only a rough indication of the extent and direction of reaction; although addition and nucleophilic substitution require up to 1 and 2 moles of alkali per mole of base respectively, paucity of knowledge of p$K_a$ values of amines and amino-acids in aqueous dioxan together with the competing hydrolysis of benzoyl *iso*thiocyanate preclude any quantitative assessment of the results.

TABLE 2. *Reactions of benzoyl* iso*thiocyanate with amines and amino-acids.*

| Reactant | pH | Alkali uptake (mole/mole of amine) | *N*-Benzoyl compound % | *N*-Benzoyl compound M. p. | *N*-Benzoylthiocarbamoyl compound % | *N*-Benzoylthiocarbamoyl compound M. p. |
|---|---|---|---|---|---|---|
| Glycine | 8·5 | 2·23 | 84 | 186·5—187·0° | 0 | — |
| Methylamine | 8·5 | 1·79 | 9 | 79 | 5 | 147·0—147·5° |
| α-Alanine | 8·5 | 1·63 | 90 | 162·5—163·0 | 0 | — |
| β-Alanine | 9·5 | 1·69 | 78 | 132·0—132·5 | 0 | — |
| γ-Aminobutyric acid | 8·5 | 1·60 | 17 | 88·5—89·0 | 0 | — |
| 6-Aminohexanoic acid | 8·5 | 1·65 | 49 | 80—81 | 5 | 127·5—128·0 |
| Norleucine | 8·5 | 1·57 | 73 | 132—133 | 0 | — |
| Glycylglycine | 7·0 | 1·64 | 76 | 204·5—206·0 | 7 | 221 * |
| *p*-Aminobenzoic acid | 8·5 | 0·07 | 0 | — | ~100 | 226—227 * |
| Anthranilic acid | 8·5 | 0·10 | 0 | — | ~100 | 160—161 |
| *N*-Phenylglycine | 8·5 | 0·23 | 0 | — | ~100 | 168·5—169·0 |
| 1-Amino*cyclo*hexanecarboxylic acid | 8·5 | 1·03 | 0 | — | 25 | 194·0—194·5 |
| *cyclo*Hexylamine | 8·5 | 0·65 | 21 | 147—148 | 53 | 71—72 |
| ,, (in $C_6H_6$) | — | — | 0 | — | 76 | 71—72 |

* Decomp.

A nucleophilic substitution involving benzoyl *iso*thiocyanate and an amine should be favoured (i) in a highly polar solvent such as water, and (ii) by using an amine of high p$K_a$, providing that it is appreciably dissociated at the pH of the reaction. Our results, as well as experiments recorded by Dixon and Taylor,[6] indicate that both factors must be operative for benzoylation to occur. Thus, for example, no *N-cyclo*hexylbenzamide was detected when benzoyl *iso*thiocyanate and *cyclo*hexylamine interacted in benzene, but 21% was isolated after reaction in aqueous dioxan at pH 8·5. Further, in aqueous dioxan anthranilic acid, *p*-aminobenzoic acid, and *N*-phenylglycine, which are weak bases, reacted exclusively by addition.

There are several indications that a carboxylate ion in proximity to the amino-group favours acylation, but it is not known whether this results from acceleration of substitution

or retardation of addition. Thus, α-amino-acids, with the exception of 1-amino*cyclo*hexanecarboxylic acid, gave no *N*-benzoylthiocarbamoyl derivatives in aqueous dioxan at pH 8·5, whereas 6-aminohexanoic acid afforded a small amount. The formation of a little *N*-benzoylthiocarbamoylglycylglycine from the peptide may result from this effect or from the relatively low p$K_a$ of the amino-group. The presence of benzoate ion did not favour benzoylation, since in parallel experiments with *cyclo*hexylamine and benzoyl *iso*thiocyanate in aqueous dioxan at pH 8·5, addition of benzoic acid gave a slightly inferior yield of *N-cyclo*hexylbenzamide. It is also instructive to compare the results of experiments with glycine and methylamine under comparable conditions. As mentioned above, most of the methylamine was unchanged, but *N*-benzoyl-*N'*-methylthiourea (5%) was isolated in addition to *N*-methylbenzamide (9%), whereas glycine yielded hippuric acid (84%) only. A similar attempt to compare the reactions of benzoyl *iso*thiocyanate with *n*-butylamine in aqueous dioxan with that involving norleucine failed, because the products from the amine were oils which could not be satisfactorily purified. This is not surprising, since *N-n*-butylbenzamide and *N*-benzoyl-*N'-n*-butylthiourea both have low m. p.s and inconveniently high solubilities in organic solvents. A surprising anomaly is seen in the experiments involving *cyclo*hexylamine and 1-amino*cyclo*hexanecarboxylic acid. The good recovery of amide and thiourea, which resulted from the reaction of *cyclo*hexylamine with benzoyl *iso*thiocyanate in aqueous dioxan, was not unexpected since, although the p$K_a$ of *cyclo*hexylamine in water is 10·64, the apparent p$K_a$ in 50% aqueous ethanol is 9·83. The only product isolated, albeit in low yield, from the reaction of 1-amino*cyclo*hexanecarboxylic acid with benzoyl *iso*thiocyanate, however, was 1-(*N*-benzoylthiocarbamoyl)amino*cyclo*hexanecarboxylic acid.

It is clear that benzoyl *iso*thiocyanate is an unsuitable reagent for procuring the stepwise degradation of peptides through their *N*-benzoylthiocarbamoyl derivatives. It seemed possible, however, than aroyl *iso*thiocyanates with bulky substituents in the *ortho*-positions might react preferentially by addition, owing to steric retardation of nucleophilic substitution at the carbonyl-carbon atom. It is noteworthy that the methanolysis of benzoyl chloride [8] at 0° is 142 times faster than that of 2 : 4 : 6-tribromobenzoyl chloride at 25°. Several attempts to isolate the acyl *iso*thiocyanate after reaction between potassium thiocyanate and 2 : 4 : 6-tribromobenzoyl chloride in acetonitrile were unsuccessful, although potassium chloride was precipitated quantitatively. The product was usually an insoluble, amorphous, yellow solid with indefinite m. p. and was probably polymeric. The existence of the acyl *iso*thiocyanate in solution was established, however, by isolation, in good yield, of its addition products with aniline and *cyclo*hexylamine. Addition also occurred rapidly with glycine and glycylglycine in aqueous acetonitrile at alkaline pH, and the corresponding *N*-2 : 4 : 6-tribromobenzoylthiocarbamoyl derivatives were isolated in approximately 80% yield. The value of this and similar 2 : 6-disubstituted aroyl *iso*thiocyanates as reagents for peptide degradation remains to be ascertained.

## Experimental

Peroxide-free dioxan [9] was used. Experiments at constant pH were performed with a Radiometer type TTTl pH-stat and magnetic valve. Benzoyl *iso*thiocyanate was prepared by heating benzoyl chloride (56·5 g.) and potassium thiocyanate (45 g.) in dry acetone (200 c.c.) under reflux for 1 hr. After cooling and filtration, benzene (300 c.c.) was added to the filtrate, and the mixture kept for 1 hr., filtered, and evaporated under reduced pressure below 40°. Distillation through a short column of glass helices furnished the pure product (30—40 g.), b. p. 58—62°/0·03 mm., which solidified during storage in a desiccator at −20°.

*N-Benzoyl-N'-cyclohexylthiourea.*—Reaction of benzoyl *iso*thiocyanate (0·81 g.) and *cyclo*hexylamine (0·5 g.) in benzene (10 c.c.) afforded an oil which soon solidified. After crystallisation from ethanol, the product (1·02 g.) had m. p. 71—72° (Found: C, 63·9; H, 6·6; N, 11·2. $C_{14}H_{18}ON_2S$ requires C, 64·0; H, 6·9; N, 10·7%).

[8] Norris and Young, *J. Amer. Chem. Soc.*, 1935, **57**, 1420.
[9] Eigenberger, *J. prakt. Chem.*, 1931 **130**, 75.

XUM

N-*Benzoyl*-N′-n-*butylthiourea*.—This *compound* (68%), prepared as above, separated after addition of much light petroleum (b. p. 40—60°) and storage at −20°. Recrystallised from light petroleum (b. p. 40—60°), it had m. p. 51—52° (Found: C, 61·0; H, 6·7; N, 12·2; S, 13·1. $C_{12}H_{16}ON_2S$ requires C, 61·0; H, 6·8; N, 11·8; S, 13·6%).

*N*-*n*-Butylbenzamide was obtained as a colourless oil from the interaction of benzoyl chloride and *n*-butylamine in 2N-sodium hydroxide. After storage at 0° and $10^{-2}$ mm. over phosphoric oxide and paraffin wax, it solidified and was recrystallised from *cyclo*hexane–light petroleum (b. p. 40—60°) or ethyl acetate–light petroleum (b. p. 40—60°) (1 : 19); it had m. p. 39·5—40·5°. This compound has been variously described as an uncrystallisable oil,[10] and as a solid [11, 12] with m. p. 41—42° or 68—70°.

*Hydrolysis of Benzoyl* iso*Thiocyanate*.—(i) Agitation of a mixture of benzoyl *iso*thiocyanate, water, and ether for 3 weeks, followed by fractionation with aqueous sodium hydrogen carbonate, afforded benzamide (81·5%) and benzoic acid (3%).

(ii) Experiments at constant pH are summarised in Table 1. At the end of the reaction (12—18 hr.), the mixture was acidified to pH 2 and concentrated under reduced pressure. The insoluble fraction was collected, and the filtrate was extracted continuously with ether overnight. The insoluble fraction and the ether extract were combined and shaken with saturated sodium hydrogen carbonate. Benzoic acid was isolated from the aqueous phase. After evaporation of the ether extract, the residue was fractionally crystallised from aqueous ethanol. Purity of the amides was checked by m. p. alone and in admixture with authentic specimens, by examination of infrared spectra and by paper chromatography in benzene–acetic acid–water (1 : 1 : 1) and *cyclo*hexane–propan-2-ol–90% acetic acid (65 : 15 : 20) followed by detection with a low-pressure mercury-vapour lamp (2537 Å). Alternatively, as in the last experiment in Table 1, dibenzoylamine was isolated by evaporation of the alkaline reaction mixture under reduced pressure. Acidification furnished a mixture of benzamide and benzoic acid, which was resolved by partition between ether and saturated sodium hydrogen carbonate.

*Reactions of Benzoyl* iso*Thiocyanate with Amino-acids and Amines*.—Generally, the amino-acid (0·01 mole) and benzoyl *iso*thiocyanate (0·010—0·011 mole) were allowed to react in 50% aqueous dioxan at the desired pH. After acidification with hydrochloric acid to pH 1, the solution was concentrated under reduced pressure, and the product was collected and recrystallised. The results of these experiments are summarised in Table 2; experiments which afforded two products or new compounds are described in more detail below.

(i) 6-*Aminohexanoic acid*. Reaction of 6-aminohexanoic acid (1·31 g.) and benzoyl *iso*thiocyanate (1·63 g.) gave a solid, which was separated by fractional crystallisation first from ethyl acetate–light petroleum (b. p. 40—60°) and then from aqueous ethanol into 6-benzamidohexanoic acid (1·01 g.), having m. p. and mixed m. p. 80—81°, and 6-(*N-benzoylthiocarbamoyl*)*aminohexanoic acid* (0·14 g.), m. p. 127·5—128·0° (Found: C, 57·2; H, 6·1; N, 9·5. $C_{14}H_{18}O_3N_2S$ requires C, 57·1; H, 6·2; N, 9·5%).

(ii) *Glycylglycine*. Reaction of the peptide (1·32 g.) and benzoyl *iso*thiocyanate (1·63 g.) afforded hippuroylglycine (2·09 g.), m. p. and mixed m. p. 204·5—206·0°, and *N*-benzoylthiocarbamoylglycylglycine (0·21 g.), m. p. 221° (decomp.) undepressed by admixture with an authentic sample and having an identical infrared spectrum. The insolubility of the latter compound in hot ethanol afforded a ready method of separation.

(iii) 1-*Amino*cyclo*hexanecarboxylic acid*. The amino-acid (1·43 g.) and benzoyl *iso*thiocyanate (1·63 g.) afforded 1-(*N-benzoylthiocarbamoyl*)*amino*cyclo*hexanecarboxylic acid* (0·77 g.), which had m. p. 194·0—194·5° after two recrystallisations from aqueous ethanol (Found: C, 59·0; H, 6·1; N, 9·6. $C_{15}H_{18}O_3N_2S$ requires C, 58·8; H, 5·9; N, 9·1%).

(iv) *Methylamine*. After completion of the reaction between methylamine and benzoyl *iso*thiocyanate, the solution was evaporated under reduced pressure, diluted, and filtered. The gummy residue, twice recrystallised from aqueous ethanol, afforded *N*-benzoyl-*N*′-methylthiourea (5%), m. p. and mixed m. p. 149—150°. The filtrate was evaporated under reduced pressure and twice evaporated with ethanol. An ethanolic extract of the residue was filtered from sodium chloride and evaporated. Ether-extraction left a residue of unchanged methylamine hydrochloride (79%). Removal of ether furnished *N*-methylbenzamide (9%), m. p. and mixed m. p. 79° after two recrystallisations from benzene–light petroleum (b. p. 40—60°).

[10] Coleman and Howells, *J. Amer. Chem. Soc.*, 1923, **45**, 3084.
[11] Grimmel, Guenther, and Morgan, *ibid.*, 1946, **68**, 539.
[12] Braun and Weismantel, *Ber.*, 1922, **55**, 3165.

(v) cyclo*Hexylamine*. After interaction of this base and benzoyl *iso*thiocyanate in 66% aqueous dioxan, acidification and evaporation under reduced pressure gave an oil, which solidified after storage at 0°. Fractional crystallisation first from benzene–light petroleum (b. p. 90—120°) and then from aqueous ethanol yielded *N-cyclo*hexylbenzamide (21%), m. p. and mixed m. p. 147—148°, and *N*-benzoyl-*N'-cyclo*hexylthiourea (53%), m. p. 71—72° alone and in admixture with the sample described above.

N-cyclo*Hexyl*-N'-2 : 4 : 6-*tribromobenzoylthiourea*.—A solution of 2 : 4 : 6-tribromobenzoyl chloride (0·36 g.) and dry potassium thiocyanate (0·11 g.) in acetonitrile (5 c.c.) was heated under reflux for 30 min., cooled, and filtered. The residue was washed with acetonitrile, and *cyclo*hexylamine (0·10 g.) was added to the combined filtrates. After 2 hr., solvent was removed under reduced pressure, and the residue was leached with hot ethyl acetate. The extract was evaporated and kept at −20°; the *product* (0·36 g.), after recrystallisation from ethyl acetate–benzene (1 : 9), melted unsharply at 250—265°, resolidified, and decomposed above 280° (Found: C 34·1; H 3·2; N, 5·8. $C_{14}H_{15}ON_2Br_3S$ requires C, 33·7; H, 3·0; N, 5·6%).

N-*Phenyl*-N'-2 : 4 : 6-*tribromobenzoylthiourea*.—Similarly prepared in theoretical yield, this *compound* had m. p. 213·5—214·5° after recrystallisation from aqueous acetone (Found: C, 34·0; H, 2·1; N, 5·8. $C_{14}H_9ON_2Br_3S$ requires C, 34·1; H, 1·8; N, 5·7%).

N-2 : 4 : 6-*Tribromobenzoylthiocarbamoylglycine*.—A solution of 2 : 4 : 6-tribromobenzoyl *iso*thiocyanate (0·01 mole) in acetonitrile (40 c.c.), prepared as above, was allowed to react with glycine (0·005 mole) in water (20 c.c.) and acetonitrile (20 c.c.) at pH 8·5 (alkali consumption 0·0054 mole). The solution was acidified and concentrated to small bulk, and the residue was partitioned between saturated sodium hydrogen carbonate and ethyl acetate. The aqueous layer, after two further washes with ethyl acetate and acidification, afforded N-2 : 4 : 6-*tribromobenzoylthiocarbamoylglycine* (1·9 g.), m. p. 228—230° (Found: C, 26·5; H, 2·1; N, 6·0. $C_{10}H_7O_3N_2Br_3S,\frac{1}{2}C_2H_5{\cdot}OH$ requires C, 26·5; H, 2·0; N, 5·6%).

N-2 : 4 : 6-*Tribromobenzoylthiocarbamoylglycylglycine*.—This was prepared from glycylglycine by the method described for the foregoing compound, except that the reaction was conducted at pH 7 (alkali consumption 0·92 mole/mole of peptide). The *product* had m. p. 214·5—215·5° (from ethanol) (Found: C, 27·3; H, 2·2; N, 8·4. $C_{12}H_{10}O_4N_3Br_3S$ requires C, 27·0; H, 1·9; N, 7·9%).

The authors thank Mrs. W. Fletcher for technical assistance, and Imperial Chemical Industries Limited for financial assistance.

STAVELEY RESEARCH LABORATORIES,
THE UNIVERSITY, SHEFFIELD, 10. [*Received, November 12th*, 1957.]

---

## 224. 5-*Alkylacridines. Part I. Synthesis of 5-Methylacridine and Certain Substituted Analogues.*

By A. CAMPBELL, C. S. FRANKLIN, E. N. MORGAN, and D. J. TIVEY.

A new synthesis of 5-methylacridine is described. Reaction of 5-chloroacridine with ethyl malonate and degradative hydrolysis of the product afforded 5-methylacridine in high yield. This and certain of its homologues with *N*-bromosuccinimide gave the reactive 5-bromomethyl compounds. Syntheses of 5-(*N*-dichloroacetyl-*N*-2-hydroxyethylaminomethyl)acridine (V) and 2-chloro-7-methoxy-5-(4-diethylamino-1-methylbutylaminomethyl)-acridine (IX) are also described.

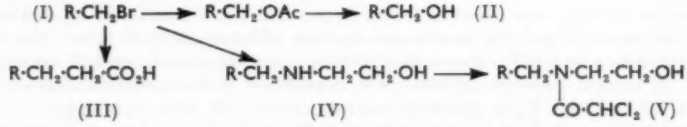
IN a chemotherapeutic investigation certain substituted 5-methylacridines have been prepared. Existing syntheses [1] of the versatile intermediate 5-methylacridine and certain of its homologues are unsuitable for large-scale preparation and give poor yields. Condensing 5-chloroacridine with diethyl malonate in presence of sodium ethoxide and

[1] Albert, "The Acridines," Edward Arnold & Co., London, 1951, p. 128.

hydrolysing intermediate ethyl acridinylmalonate *in situ* by acid gave 5-methylacridine in almost quantitative yield:

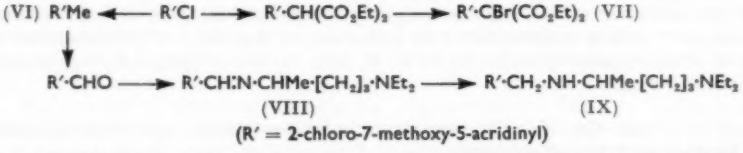
$$RCl \longrightarrow R{\cdot}CH(CO_2Et)_2 \longrightarrow RMe\ (R = 5\text{-acridinyl})$$

5-Methylacridine with *N*-bromosuccinimide furnished the reactive bromomethyl compound (I). With potassium acetate this gave 5-acetoxymethylacridine, which was hydrolysed to 5-hydroxymethylacridine (II), and with sodio-malonic ester gave, after hydrolysis, 2-5′-acridinylpropionic acid (III).



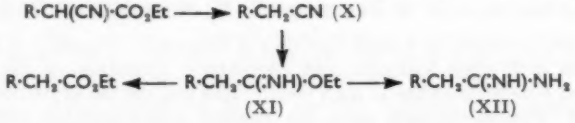

Recent publications [2,3] describing the amœbicidal activity of certain *N*-benzyl-*N*-hydroxyalkyldichloroacetamides prompted the synthesis of an acridine isostere. 5-Bromomethylacridine and ethanolamine in chloroform yielded 5-(2′-hydroxyethylaminomethyl)-acridine (IV). This, on treatment with dichloroacetyl chloride, gave the amide (V), an analogue which proved to be less active than other known substituted heterocyclic halogenoacetamides.[4]

Synthesis of a mepacrine analogue, carrying an intervening $-CH_2-$ link between the nucleus and the side-chain, could not be achieved *via* a corresponding 5-bromomethyl intermediate. 2-Chloro-7-methoxy-5-methylacridine (VI) was not brominated by *N*-bromosuccinimide in the manner expected. Further, although the intermediate diethyl




2-chloro-7-methoxy-5-acridinylmalonate was brominated to give the ester (VII), this did not react with 4-amino-*NN*-diethylpentylamine in a controllable manner. The successful synthesis, established in the quinoline series,[5] involved catalytic reduction of the anil (VIII), derived from 2-chloro-5-formyl-7-methoxyacridine [6] and the diamine, and gave the 2-chloro-7-methoxy-5-(4-diethylamino-1-methylbutylaminomethyl)acridine (IX), isolated as a trihydrochloride. The much lower antimalarial activity of the latter compound reflected experience with this type of compound in the quinoline field.[5]

Mild alkaline hydrolysis of ethyl 5-acridinylcyanoacetate [7] furnished 5-cyanomethylacridine (X), synthesised earlier from 5-methylacridine, phenyl-lithium, and *N*-cyano-*N*-




methylaniline.[8] Alcoholic hydrogen chloride converted 5-cyanomethylacridine into the imidoate (XI) which with alcoholic ammonia gave 5-amidinomethylacridine (XII) and, on hydrolysis, ethyl 5-acridinylacetate.

[2] Surrey, *J. Amer. Chem. Soc.*, 1954, **76**, 2214.
[3] Surrey and Rukwid, *ibid.*, 1955, **77**, 3798.
[4] Elslager, Benton, Short, and Tendick, *ibid.*, 1956, **78**, 3453.
[5] Work, *J.*, 1942, 426.
[6] Perrine and Sargent, *J. Org. Chem.*, 1949, **14**, 583.
[7] Goldberg and Kelly, B.P. 600,354/1948.
[8] Lettré, Jungmann, and Salfeld, *Chem. Ber.*, 1952, **85**, 397.

## Experimental

*Diethyl 5-Acridinylmalonate.*—A solution of the sodio-derivative from ethyl malonate (100 g., 0·62 mol.) and sodium (13·8 g., 0·6 g.-atom) in absolute ethanol (255 c.c.) was treated with 5-chloroacridine (86 g., 0·4 mol.) (irritant) and refluxed with stirring for 16 hr. Pouring the mixture into water–hydrochloric acid (1 : 1; 800 c.c.) gave a solid hydrochloride and this, when treated in aqueous solution with 2N-sodium hydroxide, afforded a crude base. Recrystallisation of the latter from light petroleum (b. p. 80—100°) gave pale yellow flattened needles of *diethyl 5-acridinylmalonate* (101·9 g., 75%), m. p. 101—102° (Found: C, 71·3; H, 5·6; N, 4·2. $C_{20}H_{19}O_4N$ requires C, 71·2; H, 5·7; N, 4·2%).

Similarly prepared, *diethyl 2-chloro-7-methoxy-5-acridinylmalonate* (65%), m. p. 115°, recrystallised from ethanol in stout needles (Found: C, 62·7; H, 5·1; N, 3·6. $C_{21}H_{20}O_5NCl$ requires C, 62·8; H, 5·0; N, 3·5%).

*5-Methylacridine.*—(i) In the foregoing preparation of diethyl acridinylmalonate, the 5-chloroacridine (86 g.) in hot toluene (255 c.c.) was added to the ethyl sodiomalonate in ethanol, and the mixture refluxed for 16 hr. After the addition of water–hydrochloric acid (1 : 1; 800 c.c.) the ethanol and toluene were distilled off, and the resultant aqueous solution refluxed for 4 hr. More water (800 c.c.) was then added and the solution filtered (charcoal) hot. The filtrate slowly deposited crystalline 5-methylacridine hydrochloride. The latter in water (2 l.) was treated with sufficient 2N-sodium hydroxide to precipitate the crude base. Recrystallisation from ethyl acetate gave pure 5-methylacridine (72 g., 92·7%), m. p. 115—116°.

(ii) Ethyl 5-acridinylmalonate (1 g.) was refluxed in aqueous hydrochloric acid (1 : 1; 6 c.c.) for 4 hr. and kept overnight. The hydrochloride which crystallised (0·94 g.), when dissolved in water and basified with ammonia, furnished the crude base (0·55 g., 96%). Recrystallisation from light petroleum (b. p. 40—60°) gave 5-methylacridine, m. p. 115—116°.

The following *acridines* were prepared as in method (i):

*3-Chloro-5-methyl-* (72%), m. p. 124—125°, pale yellow elongated plates from ethanol (Found: C, 73·3; H, 4·6; N, 6·2. $C_{14}H_{10}NCl$ requires C, 73·8; H, 4·4; N, 6·2%). The *hydrochloride* separated from water in needles, m. p. ~250° (decomp.) (Found: C, 63·4; H, 4·2; N, 5·4. $C_{14}H_{11}NCl_2$ requires C, 63·6; H, 4·2; N, 5·3%).

*2 : 8-Dichloro-5-methyl-* (70%), m. p. 214°, yellow needles from ethanol (Found: C, 63·8; H, 3·6; N, 5·5. $C_{14}H_9NCl_2$ requires C, 64·1; H, 3·5; N, 5·3%).

2-Chloro-7-methoxy-5-methyl- (VI) (77%), m. p. 169°, pale yellow needles from ethanol. Perrine and Sargent [6] record m. p. 169—170°.

*5-Bromomethylacridine* (I).—5-Methylacridine (39·5 g.) and *N*-bromosuccinimide (34 g.) were refluxed in carbon tetrachloride (770 c.c.) in presence of benzoyl peroxide (2 g.) for 4·5 hr. Filtration and storage at room temperature led to a crystalline precipitate (36 g.), m. p. 145—160° (decomp.). Recrystallisation of this from carbon tetrachloride gave pale yellow plates (slowly) of *5-bromomethylacridine*, m. p. 169—170° (decomp.), resolidifying immediately (Found: C, 61·5; H, 3·7; N, 5·3; Br, 29·1. $C_{14}H_{10}NBr$ requires C, 61·8; H, 3·7; N, 5·2; Br, 29·4%).

Similarly prepared, *5-bromomethyl-3-chloroacridine* (Found: C, 54·5; H, 3·3. $C_{14}H_9NClBr$ requires C, 54·8; H, 3·2%) recrystallised from carbon tetrachloride in pale yellow needles, decomp. >200°.

*Diethyl α-Bromo-2-chloro-7-methoxy-5-acridinylmalonate* (VII).—Diethyl 2-chloro-7-methoxy-5-acridinylmalonate (1 g.) was heated under reflux with *N*-bromosuccinimide (0·42 g.) in carbon tetrachloride (100 c.c.) for 2 hr. Next morning the mixture was filtered and evaporated. The residue recrystallised from light petroleum (b. p. 80—100°), to give needles of *bromo-ester*, m. p. 137° (Found: C, 52·6; H, 4·1; N, 3·0. $C_{21}H_{19}O_5NBrCl$ requires C, 52·5; H, 4·0; N, 2·8%).

*5-Hydroxymethylacridine* (II).—5-Bromomethylacridine (2 g.) and potassium acetate (2 g.) were refluxed in absolute ethanol (20 c.c.) for 2 hr. The cooled mixture was then poured into water (100 c.c.), and the suspension shaken with ether. Crystallisation of the ether-residue from aqueous alcohol gave pale yellow needles of *5-acetoxymethylacridine* (1·4 g.), m. p. 124° (Found: C, 76·3; H, 5·2; N, 5·5. $C_{16}H_{13}O_2N$ requires C, 76·5; H, 5·2; N, 5·6%). Hydrolysis of the acetoxy-compound (1·4 g.) in ethanol (100 c.c.) containing N-sodium hydroxide (18 c.c.), at room temperature for 17 hr., gave *5-hydroxymethylacridine* (0·8 g.), m. p. 164—165° (decomp.) (preheated to 158°) (Found: C, 80·0; H, 5·4; N, 6·7. $C_{14}H_{11}ON$ requires C, 80·3; H, 5·3; N, 6·7%).

*β-5-Acridinylpropionic Acid.*—5-Bromomethylacridine (1·36 g., 0·005 mole) was stirred into

a solution of ethyl sodiomalonate (0·01 mole) in absolute ethanol (15 c.c.), and the mixture refluxed for 1 hr. Water–hydrochloric acid (1 : 1; 20 c.c.) was then added and the ethanol removed by distillation. The resulting aqueous solution was refluxed for 4 hr., then cooled in ice and filtered to give a yellow crystalline product (1·4 g.). The latter was dissolved in water containing a little hydrochloric acid, and aqueous potassium carbonate [3 g., in water (15 c.c.)] added to the solution. After a few minutes' cooling, the suspension was filtered and the solid recrystallised from acetic acid, to give yellow needles of β-5-acridinylpropionic acid, m. p. 305° (decomp.). Jensen and Howland [9] record m. p. 310° (decomp.). The *methyl ester* recrystallised from aqueous ethanol in pale yellow plates, m. p. 92—93° (Found: C, 77·8; H, 6·3; N, 5·1. $C_{18}H_{17}O_2N$ requires C, 77·4; H, 6·1; N, 5·0%).

Similarly prepared β-*3-chloro-5-acridinylpropionic acid*, m. p. 263° (decomp.) (Found: C, 66·7; H, 4·3. $C_{16}H_{12}O_2NCl$ requires C, 67·2; H, 4·4%), recrystallised from acetic acid in yellow needles. The *ethyl ester*, b. p. 197—198°/0·4 mm., recrystallised from light petroleum (b. p. 40—60°) in yellow needles, m. p. 59° (Found: C, 68·4; H, 5·1. $C_{18}H_{16}O_2NCl$ requires C, 68·9; H, 5·1%).

5-(*2-Hydroxyethylaminomethyl*)*acridine* (IV).—5-Bromomethylacridine (35 g.) in chloroform (500 c.c.) was treated with ethanolamine (100 c.c.) and kept at room temperature overnight, then washed with water and the chloroform layer evaporated. Recrystallisation of the residue from chloroform–light petroleum (b. p. 60—80°) gave straw-coloured needles of 5-(*2-hydroxyethylaminomethyl*)*acridine* (24 g.), m. p. 133—134° (decomp.) (Found: C, 70·6; H, 6·8; N, 10·7. $C_{16}H_{16}ON_2,H_2O$ requires C, 71·1; H, 6·7; N, 10·4%).

5-(*N-Dichloroacetyl-N-2-hydroxyethylaminomethyl*)*acridine* (V).—Dichloroacetyl chloride (5 g.) was added, with cooling, to a solution of 5-(2-hydroxyethylaminomethyl)acridine (10 g.) in chloroform (250 c.c.) and kept overnight at room temperature. The resultant precipitate was collected, dissolved in water, and treated with aqueous sodium hydrogen carbonate, to give 5-(*N-dichloroacetyl-N-2-hydroxyethylaminomethyl*)*acridine* (6·5 g.), m. p. 174° (decomp.), which recrystallised in pale yellow needles from dimethylformamide (Found: C, 59·3; H, 4·3; N, 7·5. $C_{18}H_{16}O_2N_2Cl_2$ requires C, 59·5; H, 4·4; N, 7·7%).

*2-Chloro-7-methoxy-5-(4-diethylamino-1-methylbutylaminomethyl)acridine Trihydrochloride* (IX).—2-Chloro-5-formyl-7-methoxyacridine [6] (7 g.), suspended in benzene (130 c.c.), and 4-amino-*NN*-diethylpentylamine (8 c.c.) were refluxed together for 2 hr., then kept overnight. The residue obtained on complete removal of the benzene recrystallised from light petroleum (b. p. 60—80°), to give yellow needles of the *anil* (VIII) (9·2 g.), m. p. 86—87° (Found: C, 67·5; H, 7·4; N, 9·5. $C_{34}H_{30}ON_3Cl$ requires C, 67·1; H, 7·3; N, 9·8%). The latter (9 g.), suspended in dry ethanol (150 c.c.), was reduced catalytically in presence of platinum [prepared *in situ*, from platinum oxide (0·6 g.) in ethanol (20 c.c.), before addition of the anil suspension]. After removal of the catalyst, the filtrate was evaporated to dryness and the residual gum dissolved in 2N-hydrochloric acid (150 c.c.). On addition of a slight excess of aqueous ferric chloride the solution was boiled for 15 min. and set aside. The cold mixture was filtered, to give an unidentified red solid (1·8 g.), and the filtrate basified with excess of solid potassium carbonate. The resultant precipitate was extracted several times with acetone, and the acetone layer added to water. Extraction of this precipitate with ethyl acetate gave, on evaporation of the solvent, an oil. This, when treated with concentrated hydrochloric acid and water (1 : 1; 100 c.c.) and subsequently boiled and cooled, gave an orange microcrystalline precipitate of *2-chloro-7-methoxy-5-(4-diethylamino-1-methylbutylaminomethyl)acridine trihydrochloride* (3 g.), decomp. >160°, fusing at 245° (Found: C, 55·0; H, 6·6; N, 8·0. $C_{34}H_{39}ON_3Cl,3HCl$ requires C, 55·1; H, 6·7; N, 8·0%). A further crop (2·8 g.) was obtained on treatment of the filtrate with acetone; the infrared spectrum of this material was identical with that of the main crop. Attempts to recrystallise the trihydrochloride were unsuccessful.

*5-Cyanomethylacridine* (X).—Ethyl 5-acridinyl-α-cyanoacetate (37 g.) was refluxed, with stirring, in 10% aqueous sodium carbonate (1500 c.c.) for 1·5 hr. The mixture deposited, at the b. p., a yellow solid (11 g.) which, when filtered off, dried, and recrystallised gave 5-cyanomethylacridine, m. p. 227—228°, in deep red plates from benzene, or fine yellow needles from methanol. Lettré, Jungmann, and Salfeld [8] record m. p. 227°.

*5-Amidinomethylacridine* (XII).—5-Cyanomethylacridine (20 g.) in dry ethanol (250 c.c.) at 0° was treated with dry hydrogen chloride until the original precipitate dissolved. The solution, at 0° (2 days), deposited the corresponding *ethyl 5-acridinylacetimidoate dihydrochloride* (XI) (20 g.),

[9] Jensen and Howland, *J. Amer. Chem. Soc.*, 1926, **48**, 1988.

m. p. 237—238° (decomp.) (Found: C, 57·0; H, 5·7; N, 8·2. $C_{17}H_{16}ON_2,2HCl,H_2O$ requires C, 57·4; H, 5·7; N, 7·9%). This (20 g.) was shaken with 8% alcoholic ammonia (60 c.c.); after *ca.* 10 min., the mixture solidified. The precipitate was filtered off and extracted with dry ethanol to give, on cooling, *5-amidinomethylacridine hydrochloride* (11·8 g.), m. p. 268—269° (Found: C, 60·2; H, 5·7; N, 14·3. $C_{15}H_{14}N_3Cl,1·5H_2O$ requires C, 60·5; H, 5·7; N, 14·1%). The foregoing imidoate dihydrochloride (0·5 g.) was boiled in water (10 c.c.) for 3 hr. When the resultant solution was made alkaline with ammonia, a buff-coloured precipitate was obtained which, when dried and recrystallised from light petroleum (b. p. 40—60°), gave pale yellow prismatic needles of *ethyl 5-acridinylacetate* (0·3 g.), m. p. 127—128° (Found: C, 76·8; H, 5·8; N, 5·3. $C_{17}H_{15}O_2N$ requires C, 76·9; H, 5·7; N, 5·4%).

The authors thank Dr. R. E. Bowman for many helpful discussions.

RESEARCH DEPARTMENT, PARKE, DAVIS AND CO. LIMITED,
HOUNSLOW, MIDDLESEX.

[*Received, November 13th*, 1957.]

---

## 225. *Polymerizations of Ethylene in the Presence of Titanium Tetrachloride and Certain Metal Alkyls.*

By J. C. McGOWAN and B. M. FORD.

Ethylene has been polymerized at 30° by means of catalysts consisting of titanium tetrachloride with an excess of either butyl-lithium or dibutylzinc. The rates of polymerization varied as the squares of the ethylene pressures: in general, they were proportional to the amount of titanium tetrachloride and independent of the amount or the nature of the metal alkyl, but when small quantities of titanium tetrachloride were used, a large excess of dibutylzinc appeared to retard the polymerization.

THE discovery [1] that, in the presence of certain catalysts, ethylene and a number of other olefins can be polymerized at low pressures is of great interest. Catalysts can be prepared from certain metal alkyls and some compounds containing elements of the fourth, fifth, and sixth sub-groups of the Periodic System. Some measurements of the rates of polymerization of olefins at constant pressures in the presence of these catalysts have been reported by Natta and his co-workers [2,3] but, apart from this, the kinetics of the polymerizations have received very little attention. The measurements, reported below, for rates of ethylene polymerizations in the presence of titanium tetrachloride and either butyl-lithium or dibutylzinc are therefore of interest.

### EXPERIMENTAL

The apparatus (Fig. 1) consisted of a glass reservoir which, at the start of each experiment, was filled with dry purified ethylene at pressure a little above atmospheric, and to which a mercury manometer was fitted. The reaction was carried out in a flask (1 l. capacity) fitted with a special stirrer, which was capable of speeds up to 2500 r.p.m. and was fitted with Neoprene oil seals so that a vacuum could be maintained with the stirrer running. A stoppered funnel with a system of taps was provided so that a liquid could be introduced into the flask; the flask could be either evacuated or filled with oxygen-free nitrogen; and the ethylene in the reservoir could be connected to the flask. The whole apparatus was kept in an air thermostat at 30°.

The titanium tetrachloride was dissolved in *n*-decane and placed in the reaction flask, which was then evacuated and swept out with the nitrogen several times. Then a solution of the metal alkyl in *n*-decane was sucked in from the funnel where it had previously been stored under nitrogen, and the flask evacuated. The vacuum was next shut off, the flask connected to the ethylene reservoir, the stirrer started, and the pressure ($p$) read on the manometer after

[1] Ziegler, Holzkamp, Breil, and Martin, *Angew. Chem.*, 1955, **67**, 541.
[2] Natta, *Chem. and Ind.*, 1957, 296.
[3] Natta, Pasquon, and Giachetti, *Angew. Chem.*, 1957, **69**, 213.

XUM

various times ($t$). The reaction was carried out at constant volume (7·37 l.) and the total amount of *n*-decane, which was carefully dried and fractionated beforehand, was arranged so that the volume of the mixture in the flask at the beginning of the reaction was 100 c.c. It was found that the rate of uptake of ethylene increased with the speed of the stirrer up to a certain speed (about 280 r.p.m. for the fastest reactions) and was independent of the speed above this. In the experiments reported below the stirring speed was 560 r.p.m.

The results of some experiments are shown in Fig. 2 and it will be seen that straight lines are obtained when $1/p$ is plotted against $t$ unless oxygen is present in the ethylene. The rate

FIG. 1.

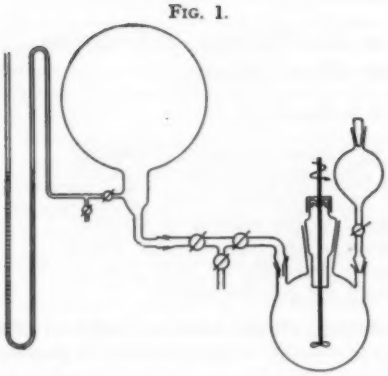
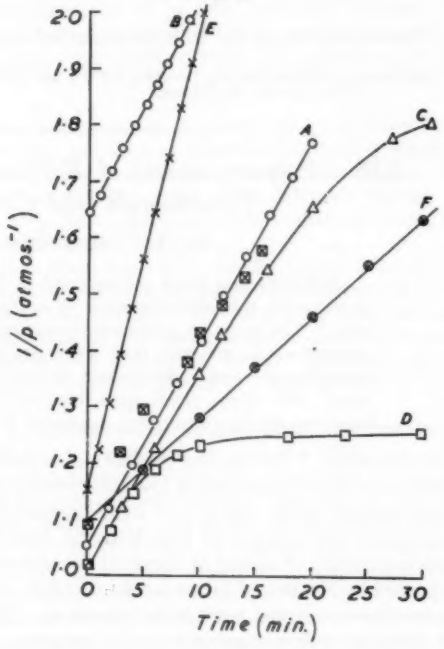


FIG. 2.




of polymerization is therefore bimolecular with respect to ethylene, for if $p$ is the partial pressure of ethylene, for a bimolecular reaction, $-\mathrm{d}p/\mathrm{d}t = kp^2$ and so

$$k(t_B - t_A) = 1/p_B - 1/p_A$$

In experiments with butyl-lithium, 0·02 mole of this and 0·005 mole of titanium tetrachloride were taken in each case. When dibutylzinc was used, the amounts of the metal alkyl and titanium tetrachloride were varied. It was found that, in general, the slopes of these lines were independent of the amount of dibutylzinc (provided an excess was used) and were proportional to the amount of titanium tetrachloride, so that

$$k^1(t_B - t_A) \times \text{moles of } TiCl_4 = 1/p_B - 1/p_A$$

Values of $k^1$ are given below (in atm.$^{-1}$ mole$^{-1}$ min.$^{-1}$) and refer to reactions in 100 c.c. of *n*-decane.

It is of interest that this relation holds for the experiments with titanium tetrachloride and butyl-lithium. It seems therefore that the rate of polymerization is proportional to the product of the square of the ethylene concentration and to the amount of titanium tetrachloride taken and is independent of the nature and quantity of metal alkyl, provided this is in excess. When the molar ratio of $TiCl_4$ : $ZnBu_2$ exceeded 1, the polymerization was usually very rapid at first but soon slowed almost to a stop; the effect was rather like that found with oxygen in the ethylene. In fact, the effect of oxygen is probably merely to use up the excess of metal alkyl.

After the polymerization had proceeded for a time, the flask containing the polymer was opened and a stream of air was passed through its contents for 15 min. The solid was then filtered off and air was sucked through it for 10 min. After this, the solid was well washed successively with hydrochloric acid, water, methanol, and ether and dried at 60° under vacuum. One g. was dissolved in boiling toluene, and the hot solution filtered through steel gauze. The solution was stored for 24 hr. and the polymer which had separated was filtered off on sintered glass and dried under high vacuum in a vessel with a jacket containin boiling toluene. The molecular weight of the polymer from experiment B141/88, from which curve $E$ was drawn, is given and discussed in a paper by Smith.[4] Some other values for the intrinsic viscosities ($\eta$) of the polymers made with titanium tetrachloride and dibutylzinc are given below. Provided an excess of dibutylzinc was used, the molecular weights of the products did not seem to vary much or to depend on any of the more obvious possible factors.

The curve $A$ in Fig. 2 is for an experiment ($k^1 = 7{\cdot}8$) with butyl-lithium and titanium tetrachloride. Curve $B$ is for a similar experiment ($k^1 = 7{\cdot}5$) started at a reduced pressure of ethylene, and the results confirmed the bimolecular law. It was found, in fact, that the rate of polymerization varies as the square of the ethylene pressure over the range 0·2—1 atm. Experiments carried out with small amounts of oxygen in the ethylene show that the reaction proceeds at much the same rate as without oxygen for a time and thereafter stops quite suddenly. The curve $C$ was obtained with 0·36% by volume of oxygen in the ethylene, and curve $D$ with 1·38%.

When the same amount of titanium tetrachloride (0·005 mole) was again taken but with 0·04 mole of dibutylzinc, the points fell close to curve $A$ and $k^1$ was 6·6. A similar rate ($k^1 = 7{\cdot}0$ and $\eta = 1{\cdot}35$) was found with 0·005 mole of titanium tetrachloride and a quarter of the amount of dibutylzinc (0·01 mole). Curve $E$ shows the effect on the rate ($k^1 = 8{\cdot}8$ and $\eta = 2{\cdot}55$) of double the concentration of titanium tetrachloride, and curve $F$ the effect on the rate ($k^1 = 8{\cdot}0$ and $\eta = 1{\cdot}69$) at half the concentration; in both experiments 0·01 mole of dibutylzinc was taken.

The above relation between pressure, time, and amount of titanium tetrachloride did not hold for experiments with small amounts of titanium tetrachloride (0·0025 mole) and relatively large amounts of dibutylzinc (0·2—0·4 mole). In these experiments, the excess of dibutylzinc appeared to be inhibiting the reaction and

$$0{\cdot}075(t_B - t_A) \times \text{moles of } TiCl_4/\text{moles of } ZnBu_2 = 1/p_B - 1/p_A$$

It is of interest that for $ZnBu_2 = 0{\cdot}01$ mole, this expression equals the one above with $k^1 = 7{\cdot}5$.

## Discussion

The polymerization of olefins in the presence of Ziegler's and related catalysts has been reviewed by Eirich and Mark,[5] who make a number of suggestions concerning the mechanism, one of which is that, in the presence of a strong reducing agent, metal alkyl compounds may be formed with monomer. It is well known that olefins can react with "Lewis acids" and it has also been suggested by Nash [6] that certain olefins can react with "Lewis bases" (*i.e.*, they can acquire electrons from reducing agents). The polymerizations described above were carried out in the presence of excess of the metal alkyl which is a very strong reducing agent. The formation of a complex by the transfer of an electron from a tervalent alkyl titanium derivative to ethylene might be one stage in the polymerization:

$$R - \overset{|}{Ti} + CH_2{:}CH_2 \rightleftharpoons [R - \overset{|}{Ti^+}][\bar{C}H_2 - \dot{C}H_2] \quad (I)$$

The complex might resemble the structures suggested by Nash, in which the negative charge and free valency are equally shared by the two carbon atoms of the ethylene, or it

[4] Smith, *J. Polymer Sci.*, 1956, **21**, 563.
[5] Eirich and Mark, *J. Colloid Sci.*, 1956, **11**, 748.
[6] Nash, *Nature*, 1957, **179**, 868.

might have at least some covalent character and approach the structure of the metal alkyl compound suggested by Eirich and Mark. The titanium in the complex is quadrivalent, and if another electron were to be given up by the complex to an ethylene molecule one of the groups attached to the titanium atom would have to be split off, since compounds of quinquevalent titanium are not known. The carbon–titanium bond is a weak one and is the likely bond to split. The following reaction suggests a possible mechanism for the polymerization:

$$[R-\overset{|}{\underset{|}{Ti^+}}][\bar{C}H_2-\dot{C}H_2]+CH_2{:}CH_2 \rightleftharpoons R^+[\overset{|}{\underset{|}{Ti^+}}][\bar{C}H_2-\dot{C}H_2]_2 \longrightarrow [R{\cdot}CH_2{\cdot}CH_2-\overset{|}{\underset{|}{Ti^+}}][\bar{C}H_2-\dot{C}H_2] \quad \text{(II)}$$

The overall rate of the polymerization consisting of reactions (I) and (II) can be proportional to the amount of titanium available and to the square of the ethylene pressure provided the equilibria are quickly established and the conversion of titanium tetrachloride into the alkyl(*i.e.*, butyl)titanium derivative is complete when there is an excess of metal alkyl.

In most cases the polymerizations seemed to be independent of the concentration of dibutylzinc used but with small quantities of titanium and large amounts of dibutylzinc, the rate seems to be inversely proportional to it. It may be that the tervalent alkyltitanium compound can combine reversibly with metal alkyl to form a bivalent dialkyltitanium derivative devoid of catalytic activity:

$$R-\overset{|}{\underset{|}{Ti}}+R^- \rightleftharpoons R-\overset{|}{\underset{|}{Ti^-}}-R \quad \text{(III)}$$

Some reaction kinetics which differ from those reported above have been mentioned by Natta,[2,3] who, however, emphasizes that his catalysts differ from ordinary Ziegler catalysts. Whereas a large number of the latter are suitable for polymerization of ethylene, only a limited number are suitable for the polymerizations of higher α-olefins, and even fewer give high yields of crystalline isotactic polymers. The useful stereospecific catalysts are completely heterogeneous and must be coarsely crystalline. It is also essential that the compound of titanium (or vanadium) should be in its lower valency state before it is mixed with the metal alkyl. The polymerizations described in the experimental section were carried out under conditions far removed from those laid down by Natta. The titanium was added in the quadrivalent state, the solid precipitated was amorphous, and the reaction may have been partly homogeneous. With a stereospecific catalyst, Natta states that the rate of polymerization is proportional to the surface area of the catalyst and to the concentration of monomer: it is independent of the concentration of metal alkyl provided this is above a certain value. In order to explain these results reported by Natta, it is only necessary to assume that the titanium on the surface of the stereospecific catalysts is so very reactive towards ethylene that, after the induction period which Natta observed, reaction (I) is complete. Reaction (III) will not then occur. The rate of polymerization will be controlled by reaction (II) and will be proportional to the product of the ethylene pressure and quantity of available titanium.

IMPERIAL CHEMICAL INDUSTRIES LIMITED,
WINNINGTON, NORTHWICH, CHESHIRE.

[*Received, August 26th*, 1957.]

## 226. *The Absorption Spectra of Some Ferrous and Ferric Complexes.*

By J. C. Tomkinson and R. J. P. Williams.

The absorption spectra of a series of complexes of 8-hydroxyquinolines (oxines) with ferrous and ferric ions have been measured. The bands in the visible region of the spectrum are specific to the cations. The changes of intensity and position of the bands are interpreted. The discussion is supported by reference to other measurements in a variety of solvents and to studies of other ligand complexes of the cations.

The visible absorption spectra of ferric and ferrous complexes have been described by Williams.[1] When the ligand itself had no absorption in the visible region the observed bands were due to the specific properties of these two cations as cations of other metals in the same type of complex did not give rise to similar bands. For a given ligand, *e.g.*, phenanthroline, a change of substituent in it produced opposed shifts in the absorption maxima of the ferrous and the ferric complex. It was concluded that the absorption was due, in part, to charge transfer either from the cation to the ligand (with ferrous ion), or from the ligand to the cation (with ferric ion). Oxinates (8-hydroxyquinoline derivatives)

Table 1. *The absorption spectra of ferric oxinates.*

| | $\lambda_A$ (mμ) | $\lambda_B$ (mμ) | $\varepsilon_A$ | $\varepsilon_B$ | | $\lambda_A$ (mμ) | $\lambda_B$ (mμ) | $\varepsilon_A$ | $\varepsilon_B$ |
|---|---|---|---|---|---|---|---|---|---|
| | In 50% dioxan–water | | | | | In 75% dioxan–water | | | |
| Oxine | 460 | 580 | 5160 | 4000 | Oxine | 462 | 580 | 5510 | 4000 |
| 2-Methyl | — | *ca.* 575 | — | 1120 | 5-Chloro | 475 | *ca.* 600 | (6490) | (4000) |
| 5-Methyl | 479 | 607 | 5840 | 4260 | 5-Bromo | 475 | 596 | (7290) | (4560) |
| 5-Fluoro | 477 | 592 | 5300 | 3790 | 5-Iodo | 475 | 605 | (8120) | (5150) |
| 5-$CO_2$Et | 450 | 583 | 9250 | 5050 | 5 : 7-Dichloro | 477 | 614 | 6280 | 4450 |
| 5-Cyano | 453 | 587 | (8650) | (5000) | 5 : 7-Di-iodo | 480 | 620 | (6830) | (4800) |
| 5-CH:N·OH | 487 | 635 | (9550) | (5000) | 7-Iodo-5-sulphonic acid | 460 | 598 | (6000) | (4930) |
| 5-Formyl | 456 | 595 | (12,700) | (6000) | 5-Sulphonic acid | 452 | 582 | (6540) | (4590) |
| Xanthurenic acid * | — | 625 | — | 5200 | 5-$CO_2$Et | 455 | 583 | 10,500 | 5600 |

Figures in parentheses are less reliable, and are derived from examination of solutions taken from titration cells after pH-titration experiments. In the other cases specially prepared solutions were used. * 4 : 8-Dihydroxyquinoline-2-carboxylic acid.

Table 2. *The absorption spectra of ferrous oxinates (room temperature) (Solvent: 50% aqueous dioxan).*

| | $\lambda_{max.}$ (mμ) | ε | Degree of formation | | $\lambda_{max.}$ (mμ) | ε | Degree of formation |
|---|---|---|---|---|---|---|---|
| Oxine | 512 | 1100 | 2 : 1 | 5-CH:N·OH | 600 | 2200 | 3 : 1 |
| | 587 | 2120 | 3 : 1 | 5-Cyano | 600 | 2700 | 3 : 1 |
| 2-Methyl | 520 | 400 | 2 : 1 | 5-Formyl | 608 | 3300 | 3 : 1 |
| 5-Methyl | 595 | 2060 | 3 : 1 | Xanthurenic acid (aq.) | 535 | 850 | 2 : 1 |
| 5-Fluoro | 605 | 1632 | 3 : 1 | | | | |

were included in the generalisation although relatively few experimental data were available. In the earlier discussion [1] the change of intensity of the visible absorption in complexes of a number of different cations, *e.g.*, nickel, cobaltous, and ferrous, with unsaturated chelating ligands led to the conclusion that two states of different electron spin, and therefore of different magnetic moment, of the same cation–ligand complex existed in equilibrium.[2] Since then other papers [3,4,5] have confirmed the suggestion. Now it will be shown that the existence of such equilibria explains the intensities of the spectra of some further ferrous and ferric complexes.

[1] Williams, *J.*, 1955, 137.
[2] Willis and Mellor, *J. Amer. Chem. Soc.*, 1947, **69**, 1237.
[3] Clark and Odell, *J.*, 1955, 3431.
[4] *Idem, ibid.*, 1956, 620.
[5] Sacconi, Paoletti, and Re, *J. Amer. Chem. Soc.*, 1957, **79**, 4062.

XUM

*Position of the Absorption Maxima in Oxinates.*—Tables 1 and 2 list the position and the intensity of the absorption maxima in a series of ferrous and ferric oxinates. The stoicheiometry of the complexes is known from their formation functions.[6]

In the ferric spectra there are two bands to be considered, at about 475 and 600 mμ, apart from those of the ligands themselves. As neither of these bands is found for oxine complexes of other tervalent cations they are attributed to the ferric ion. The two bands do not shift in the same way with change of substituent in every case. However, there is a general shift of both bands to longer wavelengths as the electron-donor character of the substituent is increased. This is in keeping with the idea that both bands are, in part, due to charge-transfer transitions to the cation. The interpretation cannot be more detailed while so little is known about the exact order of the effect produced by the individual substituents upon the σ- and π-electron density in the ligand.[7]

The band of the ferrous complexes at about 500—600 mμ is absent for other bivalent metal oxinates and is thus probably due to specific properties of the ferrous cation. It moves but slightly with change of substituent, as with the ferrous phenanthrolines.[1] The interpretation of the band shift is made difficult also by the uncertainty in the band position (±5 mμ) due to the flatness of the absorption peak, but there is little correlation with the shift for the corresponding ferric complexes. There may well be

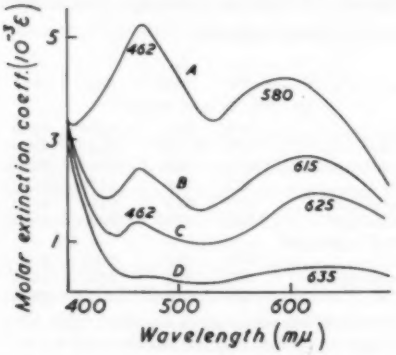



FIG. 1. *The change of absorption spectrum of ferric oxinate solutions as the degree of formation of the complex is increased.*

*A*, pH 6·0. *B*, pH 2·5
*C*, pH 2·3. *D*, pH 1·5

*Numerals on the curves are* mμ.

some charge transfer from the ferrous cation to the ligands, as has been postulated for the phenanthroline complexes,[1] but in neither case can charge transfer be such a dominant feature of the spectrum as it is for the ferric complexes.

*The Intensity of the Ferric Oxinate Absorption Bands.*—As the degree of formation of ferric oxinate is increased the intensity of absorption at 600 mμ rises roughly proportionately and moves *slightly* to shorter wavelengths (Fig. 1). The rise in intensity is similar to that for other ferric complexes, but the shift in band position is smaller in the oxinates than in the other complexes. The band at shorter wavelengths is weaker than that at longer wavelengths at low degrees of formation but increases in intensity as complex formation nears completion (see Fig. 1). It is not possible to say whether this change is common to all ferric complexes although many 3 : 1 ferric chelates have a similar two-band absorption spectra where neither band can be attributed to ligand transitions.[1] In those cases where steric hindrance prevents formation of a 3 : 1 complex, *e.g.*, with 2-methyl- and 2-carboxy-hydroxy-oxines, the short-wavelength absorption band of the ferric chelate is of very low intensity.

Table 3 gives the position and intensity of the absorption spectra of ferric oxinate in many solvents. There is hardly any change in the long-wavelength band from solvent to solvent but the short-wavelength band moves considerably and its intensity also changes

[6] Tomkinson and Williams, *J.*, in the press.
[7] Taft, *J. Amer. Chem. Soc.*, 1957, **79**, 1045.

greatly. Similar relatively large variations in intensity of this band have been noted in Table 1. The band movement with solvent shows a rough correlation with change of intensity. Bjerrum, Adamson, and Bostrup [8] have pointed out that charge-transfer bands are sensitive to solvent changes whereas *d–d* transitions are not. The effect of solvent upon the ferric band at short wave-length therefore confirms the description of it as a charge-transfer band but no similar conclusion about the other band appears to be justifiable from this evidence.

*Ferric Porphyrin Complexes.*—The above discussion of ferric oxinate spectra leads to a new assignment of the bands in ferric porphyrins. The band positions and intensities for some ferric hæmoglobin complexes are given in Table 4, together with the magnetic moments of the complexes.[9,10,11] The Soret band (410 mμ) moves to longer wavelengths as the magnetic moment falls. There is no difficulty in locating this band. The band at long wavelengths around 625—650 mμ is also readily located: it is not due to the ligand,

TABLE 3. *The spectrum of ferric oxinate in different solvents.*

| Solvent * | $\lambda_A$ (mμ) | $\lambda_B$ (mμ) | $\varepsilon_A$ | $\varepsilon_B$ | Solvent * | $\lambda_A$ (mμ) | $\lambda_B$ (mμ) | $\varepsilon_A$ | $\varepsilon_B$ |
|---|---|---|---|---|---|---|---|---|---|
| Water | 454 | 580 | 4355 | 4000 | γ-Collidine | 467 | 577 | 6780 | 4000 |
| MeOH | 459 | 578 | 5380 | 4045 | Dioxan | 466 | 572 | 6770 | 4070 |
| EtOH | 461 | 582 | 5325 | 3950 | 75% $H_2O$–dioxan | 462 | 580 | 5560 | 4000 |
| Pr$^n$OH | 463 | 582 | 5280 | 3900 | 50% $H_2O$–dioxan | 460 | 580 | 5160 | 4000 |
| Pr$^i$OH | 465 | 582 | 5450 | 3980 | 25% $H_2O$–dioxan | 457 | 580 | 4770 | 4000 |
| Bu$^n$OH | 462 | 580 | 5420 | 3950 | Nitromethane | 461 | 577 | 5420 | 3860 |
| Bu$^i$OH | 462 | 582 | 5200 | 3840 | Acetonitrile | 463 | 575 | 5870 | 4070 |
| Bu$^s$OH | 463 | 582 | 5675 | 4050 | Acetone | 463 | 573 | 6450 | 3960 |
| Bu$^t$OH | 463 | 580 | 5690 | 3950 | MeCOEt | 465 | 576 | 6390 | 3780 |
| *cyclo*Hexanol | 464 | 580 | 5520 | 4000 | Benzene | 469 | 577 | 6500 | 4035 |
| Nonan-1-ol | 463 | 582 | 5760 | 4000 | Chloroform | 468 | 585 | 5730 | 3890 |
| Pyridine | 468 | 580 | 6440 | 4070 | $CCl_4$ | 473 | 585 | 6260 | 3510 |

* The order of solvents is chosen so as to bring out obvious relations.

and is absent from other metal porphyrins, and its general behaviour suggests that it is a charge-transfer band similar to that in oxinates at 600 mμ. It falls in intensity as the magnetic moment of the complex falls. Now, in general, metal complexes of porphyrins

TABLE 4. *The absorption spectra of ferric hæmoglobin complexes* [11] ($\lambda_{max.}$ in mμ).

| Ligand | Soret band | α-Band | β-Band | Other bands | | Magnetic moment |
|---|---|---|---|---|---|---|
| Water | 404 | (575) | — | 500 | 631 | 5·65 |
| Fluoride | 403 | (565)? | (530)? | 482 | 605 | 5·76 |
| Formate | 404 | 573 | (535) | 497 | 620 | 5·44 |
| Acetate | 404 | 573 | (535) | 497 | 620 | 5·44 |
| Cyanate | 407 | 573 | — | 501 | 625 | 5·40 |
| Thiocyanate | 410 | — | — | — | 630 | 5·06 |
| Hydroxide | 409 | 575 | 540 | — | (595) | 4·66 |
| Nitro | 412 | 576 | 538 | — | (624) | 4·13 |
| Glyoxaline | 411 | 560 | 534 | — | — | 2·87 |
| Cyanide | 419 | (575) | 540 | — | — | 2·50 |
| Azide | 417 | 575 | 540 | — | (630) | 2·35 |

The bands at 500 and 625 mμ fall in intensity as those at 575 and 535 mμ rise and the magnetic moment falls. Similar results have been obtained for other ferric porphyrin complexes, *e.g.*, for a series of myoglobins.[11] Weak bands are given in parentheses.

have α- and β-bands separated by 20—30 mμ in the 520—580 mμ region of the spectrum: these bands are due to the ligands. In ferriporphyrins, *e.g.*, hæmoglobin, bands in this region are not found easily although there is usually a weak band near 570 mμ and an inflection near 540 mμ: we consider these to be the (weak) α- and β-bands. In addition

[8] Bjerrum, Adamson, and Bostrup, *Acta Chem. Scand.*, 1956, **10**, 329.
[9] Keilin and Hartree, *Biochem. J.*, 1951, **49**, 88.
[10] Hartree, *Ann. Reports*, 1946, **43**, 295.
[11] Scheler, Schoffa, and Jung, *Biochem. Z.*, 1957, **329**, 232.

XUM

there is a band at 490 mμ not common to other metal porphyrins: this shifts in a similar manner to that at 625 mμ when the protein is combined with fluoride, acetate, or formate (cf. Table 4). The bands at 490 and 625 mμ disappear when covalent ferric complexes are formed with cyanide and the usual α- and β-bands in the region of 530—570 mμ appear. Now charge-transfer bands are found only for the ionic ferric complexes. We suggest that the 480—500 mμ band is the second charge-transfer band and is similar to that in other ionic ferric chelates (oxinates) described in this paper.

A final group of ferric complexes to which we would like to refer are those of dimethylglyoxime(DMG).[12] In the complex $Fe(DMG)_3$ there are no absorption maxima above 320 mμ. In the complex $Fe(DMG)_2OH(H_2O)$, on the other hand, there is a weak band at 675 mμ and a stronger band at 460 mμ. We consider that these two bands are the charge-transfer bands expected for ionic ferric chelates. It is predicted that $Fe(DMG)_3$ will be covalent on the grounds that it does not show these bands.

*The Intensity of Absorption in Ferrous Oxinates.*—The absorption spectra of ferrous oxinates are given in Table 2. The intensity of absorption in the $Fe^{II}(Ox)^-_3$ complexes

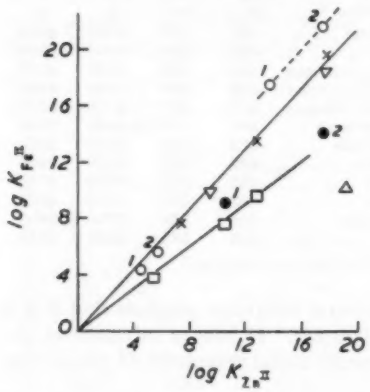



FIG. 2. *A comparison of the stability constants of a number of ferrous and zinc complexes.*

○, *Dipyridyl* (1) *and* o-*phenanthroline* (2).
●, *Nitrilotriacetate* (1) *and ethylenediaminetetra-acetate* (2).
×, *5-Formyloxinate.*
□, *Ethylenediamine.*
▽, *Acetylacetone.*
△, *Cysteine.*

The larger values refer to higher degrees of formation in each case. Note that the stronger the electron-donor the more stable the zinc complex, and the stronger the π-electron acceptor the stronger the ferrous complex (cf. Irving and Rossotti, *Acta Chem. Scand.*, 1956, **10**, 72).

rises along the series of 5-substituents, fluoro < methyl < H < CH:N·OH < cyano < formyl, which is the series of substituents of increasing π-electrophilic character.[7] Now it has been suggested that the intensity of the band at 500—600 mμ in ferrous complexes, a band absent from spectra of other cation complexes, is related to the amount of the cation which is in the diamagnetic state.[1] The existence of this type of equilibrium has been established by the study of several other transition-metal cation complexes (not oxinates) which have absorption bands at very different wavelengths.[3,4,5] We consider that there is an increase in the proportion of the ferrous ion in the diamagnetic state in the order of the above series of substituents. The substituents, in the same order as the intensity of the absorption in the ferrous complexes, are in the order which would be expected to stabilise the diamagnetic state as they are arranged according to their ability to act as π (in this case $d_\epsilon$)-electron acceptors. There is a second line of evidence which leads to the same conclusion as to the importance of these properties.

*The Relative Stability of Bivalent Cation Complexes of Oxines.*—The Irving–Williams series for the stability of complexes of bivalent cations of the first transition series is $Mn^{II} < Fe^{II} < Co^{II} < Ni^{II} < Cu^{II} > Zn^{II}$. This order is broken by the intensely coloured diamagnetic ferrous complexes of phenanthroline and dipyridyl. In the much more weakly absorbing chelate compounds of ferrous iron, *e.g.*, the parent oxinate, although the stability series is not broken, the stability of the ferrous chelate is greater than expected when compared with, for example, the zinc complex, but it does not

[12] Jillot and Williams, *J.*, 1958, 462.

exceed it in stability. This is a general observation concerning all ligands which are conjugated and form strongly coloured ferrous complexes. The only ferrous chelates known for which the stability order is $Fe^{II} > Zn^{II}$, however, are those which form diamagnetic complexes and break the stability series. Amongst substituted 8-hydroxyquinolines we have determined the stability order for 2 : 1 complexes of 5-formyloxine (Fig. 2; Tables 5 and 6). It is $Mn^{II}$, $Zn^{II} < Fe^{II} < Ni^{II}$. The ferrous chelate is stabilised relatively to zinc, but not markedly so with respect to nickel. The stabilisation can be interpreted as a stabilisation of the $d_\epsilon$-electrons by $\pi$-bond formation which, as indicated, would also stabilise the diamagnetic form of ferrous ion. For some other oxinates substituted with $\pi$-electron-acceptor groups, and particularly in pteridine complexes, Albert and Hampton [13] observed an anomalously high stability of ferrous complexes, which we take to arise in the same manner.

The step stability constants for the formation of the 1 : 1, 2 : 1, and 3 : 1 oxine complexes of these cations give further evidence. They are listed in Table 5. For 5-formyloxine the third constant is close to the other two in magnitude, which is not the case for other substituted oxinates except the 5-cyano-compound. In fact the oxinate which forms one of the least stable 1 : 1 complexes, 5-cyano, has the greatest third-step stability constant. We are unable to offer an alternative explanation to that given above, that the $d_\epsilon$-electrons are stabilised by the electron-withdrawing substituents $^-$CN and $^-$CHO.

The change in intensity of the absorption spectra of ferrous oxinates with the degree of formation of the complex is also interesting when compared with results for ferric oxinates. In the latter the intensity rises almost proportionately to the degree of formation. In ferrous chelates the intensity rises rapidly on going from the 2 : 1 to the 3 : 1

TABLE 5. *The stability constants of ferrous oxinates.* (50% Aqueous dioxan, 0·3M-sodium chloride, 25°.)

| | $\log K_1$ | $\log K_2$ | $\log K_1K_2$ | $\log K_3$ | $pk_{NH}$ | $pk_{OH}$ |
|---|---|---|---|---|---|---|
| Oxine | 8·71 | 8·12 | 16·83 | 5·3 | 4·08 | 10·82 |
| 5-Methyl | — | — | 16·90 | 6·0 | 4·24 | 11·25 |
| 2-Methyl | 8·75 | 8·35 | 17·10 | v. small | 5·05 | 11·45 |
| 5-Fluoro | — | — | 15·9 | 5·4 | 2·76 | 10·55 |
| 5-Sulphonic acid | — | — | 15·7 | 6·0 | 3·40 | 9·68 |
| 5-CH:N·OH | — | — | 14·9 | 5·3 | 3·52 | 9·22 |
| 7-Iodo-5-sulphonic acid | — | — | 13·8 | 5·0 | 1·75 | 8·13 |
| 5-$CO_2$Et | — | — | 16·2 | 5·5 | 2·88 | 8·73 |
| 5-Cyano | 7·10 | 7·15 | 14·25 | 6·0 | 2·02 | 7·85 |
| 5-Formyl | 6·90 | 6·85 | 13·75 | 5·8 | 2·51 | 7·43 |

The acid dissociation constants are " practical constants " and the stability constants are stoicheiometric constants.[14] A discussion of the change in stability of the complexes with the acid dissociation constant is given elsewhere.[15]

TABLE 6. *The step stability constants for the formation of 5-formyloxinates in 50% aqueous dioxan.*

| Metal | Ni | $Fe^{II}$ | Zn | Mn | $Fe^{III}$ |
|---|---|---|---|---|---|
| Log $K_1$ | 8·27 | 6·90 | 6·45 | 5·73 | 11·7 |
| Log $K_2$ | 7·56 | 6·85 | 6·23 | 4·97 | 10·0 |
| Log $K_3$ | 6·70 | 5·70 | 4·95 | 4·58 | 8·3 |

complex (Table 1). There is a parallel with the behaviour of the *o*-phenanthroline–ferrous complex. The extinction coefficient of the 1 : 1 ferrous–phenanthroline complex is approximately one-tenth of that of the 3 : 1 complex. It is not possible to determine the extinction coefficient of the 2 : 1 phenanthroline chelate. Another parallel between the two series is the effect of steric hindrance. The 2-methylphenanthroline–ferrous

[13] Albert and Hampton, *J.*, 1954, 505.
[14] Irving and Rossotti, *J.*, 1954, 2910.
[15] Jones, Poole, Tomkinson, and Williams, *J.*, in the press.

complex is paramagnetic and has a low extinction coefficient despite the fact that it is a tris-chelate. It has been shown that steric hindrance effectively prevents the formation of the diamagnetic complex. Amongst oxinates the extinction coefficient of the 2-methyloxine–ferrous complex is noticeably much lower than that of the other derivatives. All these facts indicate that the field due to an oxine is sufficiently strong to set up an equilibrium between diamagnetic and paramagnetic ferrous ions in which the two forms are present in similar concentrations.

*Experimental.*—The method used in the determination of stability constants has been described elsewhere.[14] Oxygen was excluded during the measurements on the ferrous complexes.[6] Absorption spectra were measured in a conventional manner with matched cells and appropriate blanks.

We thank Professors A. Albert and G. R. Clemo, Mr. R. G. Hollingshead, and Messrs. Reid Ltd. (Barking, England) for gifts of oxines; also the Royal Society for the loan of a Unicam S.P. 600 spectrophotometer. One of us is indebted to the Gas Council for a Research Fellowship. We had many helpful discussions with Dr. D. F. Evans. The Referees are thanked for much helpful comment.

THE UNIVERSITY, OXFORD. [*Received, September 30th*, 1957.]

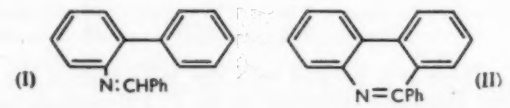
---

## 227. *Anils. Part I. Syntheses of 9-Phenylphenanthridine.*

By C. A. BARTRAM, D. HARRISON, and (the late) W. F. SHORT.

2-Benzylideneaminodiphenyl is converted into 9-phenylphenanthridine by stannic chloride in boiling *o*-dichlorobenzene or less rapidly in chlorobenzene. Phosphorus pentachloride in 1 : 2 : 4-trichlorobenzene is also a good cyclising agent, but aluminium chloride in tetrachloroethane, and phosphoryl chloride in nitrobenzene, are less effective. Rough rate measurements on the phosphorus pentachloride and stannic chloride reactions have been made, and possible reaction mechanisms are discussed. 2-Benzylaminodiphenyl with stannic chloride in boiling chlorobenzene also gave 9-phenylphenanthridine.

THE successful application [1] of the Bischler–Napieralski reaction to the synthesis of phenanthridines from 2-acylaminodiphenyls prompted us to investigate the possible extension of the Pictet–Spengler reaction to the synthesis of phenanthridines from 2-arylideneaminodiphenyls. Whilst our work was in progress, Whaley and White [2] failed to cyclise 2-aminodiphenyl by means of formaldehyde, and from 2-benzylideneamino-3′ : 4′-di- and -3′ : 4 : 4′ : 5-tetra-methoxydiphenyl with hydrogen chloride in various solvents recovered only 2-aminodiphenyl hydrochloride; these anils yielded tars on treatment with phosphoric oxide. However, Wildman and Norton,[3] by keeping 4-*m*-methoxyphenyl-5-methyleneamino*cyclo*hexene overnight with 6N-hydrochloric acid, obtained 1 : 4 : 4*a* : 9 : 10 : 10*a*-hexahydro-6-methoxyphenanthridine in 64% yield.




The present paper describes the conversion of 2-benzylideneaminodiphenyl (I) into 9-phenylphenanthridine (II) by various reagents.[4] Experiments using other anils will

[1] Morgan and Walls, *J.*, 1931, 2447.
[2] Whaley and White, *J. Org. Chem.*, 1953, **18**, 184.
[3] Wildman and Norton, *J. Amer. Chem. Soc.*, 1954, **76**, 152.
[4] Cf. B.P. Appl. 36,203/1953.

be described later. Phosphorus pentachloride in boiling 1 : 2 : 4-trichlorobenzene gave good yields of the phenanthridine (II) (cf. Table 1). A plot of these results indicates a

TABLE 1.

| Time (hr.) ..... | 1 | 2 | 4 | 6 | 7·3 |
|---|---|---|---|---|---|
| Yield (as picrate; %) | 24·4 | 33·4 | 45·4 | 64·0 | 73·6 |

first-order reaction ($k_1 \simeq 0{\cdot}17$ hr.$^{-1}$), which is consistent with rapid reaction to form an intermediate which undergoes slow cyclisation, but absence of accurate temperature control prevents further kinetic considerations. No phenanthridine was isolated from a reaction in chlorobenzene, suggesting that cyclisation of the intermediate is very slow at the boiling point of this solvent. However, hydrogen chloride was evolved rapidly and from the residue after steam-distillation 2-benzamidodiphenyl was obtained in 18% yield: since imidoyl chlorides are easily hydrolysed to amides, the intermediate may be *N*-2-diphenylylbenzimidoyl chloride. Further work on the action of phosphorus pentachloride on simple anils (*e.g.*, benzylideneaniline) is planned in order to clarify this point.

The anil (I) with stannic chloride in boiling *o*-dichlorobenzene gave the phenanthridine (II) in 72·4% yield after only 30 min. Longer heating had little effect on the yield (*e.g.*, 75·5% after 3 hr.), equilibrium apparently being attained. The method is very convenient for preparative purposes, but may have limitations with other anils. Addition of stannic chloride to the solution of the anil produced a change in colour, possibly due to complex formation; benzylideneaniline and stannic chloride give a yellow compound [5] $2CHPh{:}NPh,SnCl_4$.

Cyclisation by means of stannic chloride in chlorobenzene is rather slow for preparative use, but was studied in more detail in the hope of obtaining information about the mechanism of the reaction (cf. Table 2). The reaction follows a first-order law ($k_1$

TABLE 2. *Yields of* 9-*phenylphenanthridine picrate obtained* (*a*) *in* PhCl *and* (*b*) *in* PhCl *saturated with* HCl.

| Time (hr.) ..... | | 0·25 | 0·5 | 1·0 | 2·0 | 3·0 | 4·0 | 6·0 | 12·0 |
|---|---|---|---|---|---|---|---|---|---|
| Yield (%) ..... | (*a*) | — | 0·4 | 12·7 | 39·9 | 56·0 | 65·1 | 68·0 | 72·0 |
| | (*b*) | 9·6 | 24·1 | 33·4 | 52·0 | 61·0 | 66·4 | — | 74·9 |

$\sim 0{\cdot}34$ hr.$^{-1}$) for only the first 4 hr. and extrapolation of the appropriate plot indicates an induction period of *ca.* 30 min. during which presumably there is no cyclisation; the end of the induction period coincides roughly with the beginning of evolution of hydrogen chloride and separation of stannous chloride. This suggests that cyclisation requires the presence of a certain concentration of hydrogen chloride, normally produced by very slow reaction between the anil and stannic chloride. Table 2 shows how saturation of the chlorobenzene with hydrogen chloride reduces the induction period; and the value of $k_1$ for the first-order process occurring during the first 2 hr. is almost the same as in the absence of added hydrogen chloride. We conclude that the same species is being cyclised in each case, and a possible scheme is that illustrated.

$$(\mathrm{I}) + SnCl_4 \xrightarrow{\text{Fast}} \text{Complex} + HCl \xrightarrow{\text{Slow}} \text{9 : 10-Dihydro-compound (III)} \xrightarrow{\text{Oxidn.}} (\mathrm{II})$$

9 : 10-Dihydro-9-phenylphenanthridine (III) was obtained by reduction of 9-phenylphenanthridine with lithium aluminium hydride in tetrahydrofuran. It formed a picrate as deep red needles which became plae yellow on exposure to air or heat. The picrate of 9 : 10-dihydrophenanthridine behaved similarly.[6] 9 : 10-Dihydro-9-phenylphenanthridine with the anil (I) in boiling tetrachloroethane gave the phenanthridine (II) and 2-benzylaminodiphenyl. Hence, although other observations (see below) suggest that the compound (III) is a probable intermediate in the cyclisation, it is not isolated because it is unstable under the conditions used.

[5] Hieber and Sonnekalb, *Annalen*, 1927, **456**, 104.
[6] Bates and Cymerman-Craig, *J.*, 1954, 1153.

XUM

In the cyclisation experiments both with 4 and with 12 hours' heating, appreciable amounts of 2-aminodiphenyl and 2-benzylaminodiphenyl were isolated. The origin of the primary amine is not clear since appreciable hydrolysis of the anil, under the alkaline conditions employed in working up the reaction mixture, is not to be expected.[7] The 2-benzylaminodiphenyl would be accounted for if the oxidation step is effected partly by stannic chloride and partly by unchanged anil, which would thereby be reduced to the secondary amine. The approximate agreement with a first-order law during the early stages of the reaction suggests that conversion of the complex into the phenanthridine [probably *via* the dihydro-compound (III)] is initially the only important process, but that other reactions later supervene as 2-benzylaminodiphenyl, etc., accumulate. The present reaction is clearly more complex than that with phosphorus pentachloride.

2-Benzylaminodiphenyl with stannic chloride in boiling chlorobenzene also gave the phenanthridine (II) (cf. Table 3). First-order plots are not linear even in the early stages,

TABLE 3. *Conversion of 2-benzylaminodiphenyl into 9-phenylphenanthridine by* $SnCl_4$ *in* (*a*) PhCl *and* (*b*) PhCl *saturated with* HCl.

| Time (hr.) | | 0·25 | 0·5 | 1·0 | 2·0 | 4·0 | 6·0 | 8·0 | 12·0 |
|---|---|---|---|---|---|---|---|---|---|
| Yield (as picrate; %) | (*a*) | 5·1 | 8·5 | 17·5 | 23·2 | 31·0 | 34·4 | — | 46·7 |
| | (*b*) | — | 5·9 | 9·8 | 17·6 | 21·2 | — | 33·1 | — |

and the reaction is much slower than for the anil under the same conditions. Further, hydrogen chloride decreases the rate of formation of phenanthridine. A possible explanation is that, at least in the early stages, the reaction rate measured is the oxidation of secondary amine to anil by stannic chloride: $R{\cdot}NH{\cdot}CH_2Ph + SnCl_4 \rightleftharpoons R{\cdot}N{:}CH{\cdot}Ph + SnCl_2 + 2HCl$; hydrogen chloride should promote the reverse reaction, and hence hinder the formation of phenanthridine. Such equilibria may add a further complication to the mechanism of cyclisation of the anil discussed above.

The anil (I) with aluminium chloride in boiling tetrachloroethane gave only moderate yields (<50%) of the phenanthridine (II), probably owing to the absence of an oxidising agent. The 9 : 10-dihydro-compound formed as the initial product of cyclisation is converted into phenanthridine by unchanged anil; only half the anil would then be available for cyclisation. Similarly, phosphoryl chloride in 1 : 2 : 4-trichlorobenzene gave only very small yields of phenanthridine; use of nitrobenzene as solvent caused some improvement, perhaps owing to its oxidising properties or to formation of a complex with phosphoryl chloride; however, even under very vigorous conditions the yields were not as good as those obtained by using phosphorus pentachloride or stannic chloride.

## EXPERIMENTAL

*2-Benzylideneaminodiphenyl.*—2-Aminodiphenyl (60 g., 1 mol.) and benzaldehyde (37·6 g., 1 mol.) were heated under reflux in glacial acetic acid (90 c.c.) for 30 min. and the solvent was then removed at *ca.* 100 mm. Distillation of the residue afforded *2-benzylideneaminodiphenyl* as a pale yellow viscous oil (63·9 g., 70%), b. p. 154—157°/0·1—0·2 mm. (Found: N, 5·4. $C_{19}H_{15}N$ requires N, 5·45%). The yellow *styphnate* had m. p. 148—150° (Found: N, 11·3. $C_{25}H_{18}O_8N_4$ requires N, 11·5%).

*2-Benzylaminodiphenyl.*—2-Aminodiphenyl (67·6 g., 4 mol.) and sodium hydrogen carbonate (20·1 g., 1·25 mol.) in water (20 c.c.) were stirred and heated under reflux whilst benzyl chloride (24·3 g., 1 mol.) was added during 2 hr. The mixture was stirred overnight, cooled, and extracted with ether. The ether extract was washed with 10% sodium chloride solution, then dried ($MgSO_4$), and the ether removed. Distillation of the residue under reduced pressure and crystallisation of the product from methanol furnished prisms of *2-benzylaminodiphenyl* (15·1 g., 47%), m. p. 89—91° (Found: C, 87·7; H, 6·6; N, 5·7. $C_{19}H_{17}N$ requires C, 88·0; H, 6·55; N, 5·45%).

[7] Willi and Robertson, *Canad. J. Chem.*, 1953, **31**, 365

*Cyclisation of 2-Benzylideneaminodiphenyl.*—(a) *By phosphoryl chloride and nitrobenzene.* The anil (5·14 g., 1 mol.) in nitrobenzene (52 c.c.) was heated under reflux with phosphoryl chloride (3·07 g., 1 mol.) for 6 hr., hydrogen chloride being evolved. The dark brown mixture was evaporated under reduced pressure and the residue steam-distilled in the presence of dilute sulphuric acid (25 c.c.). The residue was made alkaline with 5N-sodium hydroxide, and the oily solid collected. A solution of it in acetone (25 c.c.) was treated with picric acid (5·18 g., 1 mol.) in acetone (25 c.c.). The 9-phenylphenanthridine picrate (4·58 g., 54%), m. p. 247—249°, which separated was collected, washed with acetone (2 × 5 c.c.), and dried *in vacuo*. Cymerman and Short [8] give m. p. 246—247°. The crude picrate was decomposed by warming it with a slight excess of an aqueous solution of lithium hydroxide. The cooled mixture was extracted with chloroform. The chloroform solution was washed with water, dried ($MgSO_4$), and evaporated, leaving 9-phenylphenanthridine (2·65 g., 51%), m. p. 102—104°. Crystallisation from light petroleum (b. p. 80—100°) raised the m. p. to 104—106°. Morgan and Walls [1] and Cymerman and Short [8] give m. p. 105—106°.

The m. p.s of the phenanthridine and its picrate, where not quoted below, were identical with those above. The volume of solvent used in all cyclisation experiments was 10 c.c. per g. of anil or amine.

(b) *By phosphoryl chloride and 1 : 2 : 4-trichlorobenzene.* The anil (1 mol.) was boiled in 1 : 2 : 4-trichlorobenzene with phosphoryl chloride (1 mol.) for 6 hr., then worked up as above. The yield of picrate was 1·8%.

(c) *By aluminium chloride and tetrachloroethane.* The anil (1 mol.) in tetrachloroethane was boiled with aluminium chloride (1 mol.) for 6 hr. The green solution was evaporated under reduced pressure and the residue steam-distilled, first in the presence of 5N-sulphuric acid (25 c.c.), and then in alkaline solution. The residue was cooled, and the solid collected and dissolved in acetone. The acetone solution gave a picrate (48·5%) from which the phenanthridine (45·0%) was regenerated as in (a). The filtrate from the picrate was evaporated, and the residue treated with warm aqueous lithium hydroxide. The mixture was extracted with chloroform, and the chloroform solution washed with water, dried ($MgSO_4$), and evaporated. Distillation of the residue gave an oil (32·6%), b. p. 172°/0·3 mm., which, crystallised from methanol, gave 2-benzylaminodiphenyl, m. p. and mixed m. p 89—91°.

(d) *By phosphorus pentachloride and chlorobenzene.* The anil (10·0 g., 1 mol.) in chlorobenzene was boiled with phosphorus pentachloride (9·7 g., 1·2 mol.) for 2 hr. Evolution of hydrogen chloride was vigorous at first, but ceased after 30 min. The mixture was evaporated under reduced pressure and the residue steam-distilled first in an acid, and then in an alkaline medium. The residual liquor was extracted with chloroform, the extract washed with water, and dried ($MgSO_4$), and the chloroform removed. The residual oil was distilled giving fractions (1), b. p. 125—150°/2—2·5 mm., and (2), b. p. 225—230°/2—2·5 mm. Fraction (1) was redistilled twice, giving a colourless oil (2·4 g.), b. p. 120—125°/1—1·5 mm. (Found: Cl, 4·1; N, 7·8%), which was not investigated further. Fraction (2), when redistilled (1·9 g.; b. p. 225—228°/1 mm.), solidified. Crystallisation from light petroleum (b. p. 60—80°) gave needles of 2-benzamidodiphenyl, m. p. and mixed m. p. 87—88°.

(e) *By phosphorus pentachloride and 1 : 2 : 4-trichlorobenzene.* The anil (1 mol.) in 1 : 2 : 4-trichlorobenzene was boiled with phosphorus pentachloride (1·2 mol.) for 6 hr. The mixture was evaporated under reduced pressure and the residue warmed on the steam-bath with 5N-sodium hydroxide for 10 min., then cooled and extracted with chloroform. The extract was washed with water, dried ($MgSO_4$), and evaporated. The residue in acetone was converted into the picrate (64%), decomposition of which gave the phenanthridine (62·4%).

(f) *By stannic chloride and o-dichlorobenzene.* The anil (1 mol.) in *o*-dichlorobenzene was boiled with anhydrous stannic chloride (2 mol.) for 15 min. As soon as boiling began, the colour changed from yellow to dark green, and stannous chloride separated. The mixture was warmed with an excess of 40% sodium hydroxide solution for 10 min., then kept at room temperature for a further hour. Extraction with chloroform, evaporation, and treatment of the residue in acetone with picric acid (1 mol.) in acetone gave the picrate (68·0%).

(g) *By stannic chloride and chlorobenzene.* The anil (1 mol.) in chlorobenzene was boiled with anhydrous stannic chloride (2 mol.) for 4½ hr. After 30 min. the mixture became dark green, and stannous chloride began to separate. The mixture, treated as in (f), gave the

[8] Cymerman and Short, *J.*, 1949, 703.

XUM

picrate (66·3%) which was decomposed to the phenanthridine (64·9%). In experiments with heating for 4·5 and 12 hr. the filtrates from the picrate were treated as in (c). Distillation, under reduced pressure, of the residues from the chloroform extracts yielded 2-aminodiphenyl (identified as the acetyl derivative) and 2-benzylaminodiphenyl (identified by mixed m. p. with an authentic specimen). The yields of these products after respectively 4½ and 12 hr. were 2-aminodiphenyl 6·6, 8·5, 2-benzylaminodiphenyl 17·9, 10·6, and 9-phenylphenanthridine 66·3, 72·0% (total recovery: 90·8; 91·1%).

(h) *By stannic chloride, chlorobenzene, and hydrogen chloride.* The anil (1 mol.) in chlorobenzene saturated with anhydrous hydrogen chloride was boiled under reflux with anhydrous stannic chloride (2 mol.) for 0·25—12 hr. By-products isolated after 4 and 12 hr. respectively, as described above, were: 2-aminodiphenyl 9·2, 4·2, 2-benzylaminodiphenyl 16·5, 13·6, and 9-phenylphenanthridine 66·4, 74·9% (total recovery: 92·1, 92·8%).

*Cyclisation of 2-Benzylaminodiphenyl.*—(*a*) 2-Benzylaminodiphenyl (1 mol.) in chlorobenzene was boiled under reflux with stannic chloride (2 mol.) for 0·25—12 hr. Isolation of 9-phenylphenanthridine picrate and treatment of the filtrate were as for the corresponding cyclisation of the anil. Yields of by-products after respectively 4 and 12 hr. were: 2-aminodiphenyl 5·6, 8·0, 2-benzylaminodiphenyl 55·0, 38·0, and 9-phenylphenanthridine 30·0, 46·7% (total recovery: 90·6, 92·7%).

(*b*) 2-Benzylaminodiphenyl (1 mol.) in chlorobenzene saturated with hydrogen chloride was boiled under reflux with stannic chloride (2 mol.) for 0·5—8 hr. The mixtures were treated as before.

9 : 10-*Dihydro-9-phenylphenanthridine.*—A suspension of lithium aluminium hydride (0·64 g., 0·8 mol.) in tetrahydrofuran (100 c.c.) was stirred and boiled under reflux. 9-Phenylphenanthridine (5·1 g., 1 mol.) in tetrahydrofuran (100 c.c.) was added during 30 min. and the heating continued for a further 24 hr. The excess of lithium aluminium hydride was destroyed by water, and the mixture poured into excess of sodium hydroxide solution and extracted with ether. The ethereal solution, which had a blue fluorescence, was dried ($MgSO_4$) and evaporated. The residual straw-coloured oil was triturated with light petroleum (b. p. 60—80°) and the nearly colourless prisms (3·62 g.), m. p. 107—111°, were collected and dried *in vacuo*. Crystallisation from ethanol gave 9 : 10-*dihydro-9-phenylphenanthridine* (2·92 g., 57%), m. p. 114—115° (Found: C, 88·6; H, 5·9; N, 5·7. $C_{19}H_{15}N$ requires C, 88·7; H, 5·8; N, 5·45%). The *acetyl derivative* separated from aqueous ethanol as needles, m. p. 138—139° (Found: N, 4·9. $C_{21}H_{17}ON$ requires N, 4·7%).

*Reaction of the Dihydrophenanthridine with 2-Benzylideneaminodiphenyl.*—9 : 10-Dihydro-9-phenylphenanthridine (2·0 g.) and 2-benzylideneaminodiphenyl (2·0 g.) in tetrachloroethane were boiled under reflux for 2½ hr. The mixture was evaporated under reduced pressure and the residue taken up in acetone (30 c.c.). With picric acid (3·6 g.) in acetone (20 c.c.) it yielded 9-phenylphenanthridine picrate (3·33 g.). Regeneration of the base with lithium hydroxide gave the phenanthridine (1·0 g.). Treatment of the filtrate from the picrate preparation as in the cyclisation experiments gave 2-benzylaminodiphenyl, m. p. and mixed m. p. 88—90°.

Thanks are offered to Dr. D. A. Peak for his advice and encouragement.

RESEARCH LABORATORIES, MESSRS. BOOTS PURE DRUG CO. LTD.,
NOTTINGHAM.
NOTTINGHAM & DISTRICT TECHNICAL COLLEGE.

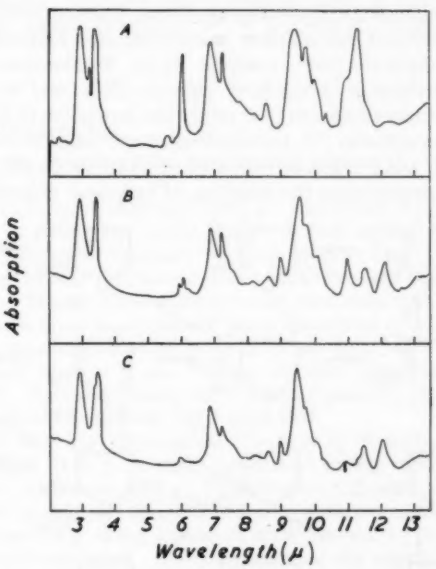
[*Received, October 8th,* 1957.]

## 228. *The Reaction of Chlorine with Tetrahydro-2-methylenefuran.*

By M. F. Ansell and D. A. Thomas.

Reaction of chlorine with tetrahydro-2-methylenefuran is shown to give 2 : 3-dichlorotetrahydro-2-methylfuran, 2-chlorotetrahydrofurfuryl chloride, 2-chlorotetrahydro-2-methylfuran, and tetrahydrofurfuryl chloride. The preparation of 4-methylpent-4-en-1-ol from 3-halogenotetrahydro-3-methylpyran is described.

The ring scission of cyclic β-halogeno-ethers by sodium to yield alkenols is well established and is applicable whether the β-halogen atom is attached to the ring [1,2,3] or to a side-chain.[4,5] The latter class of compounds is not readily available, and a possible route to one type, the addition of chlorine to tetrahydro-2-methylenefuran (VIII) followed by replacement of the α-halogen atom by an alkyl group by means of a Grignard reagent, has been investigated.




*A, 4-Methylpent-4-en-1-ol. B, Mixture of 4-methylpent-3-en-1-ol and 4-methylpent-4-en-1-ol. C, 4-Methylpent-3-en-1-ol.* Absorption at 11·27 and 6·03 μ is characteristic of $>C=CH_2$ group.

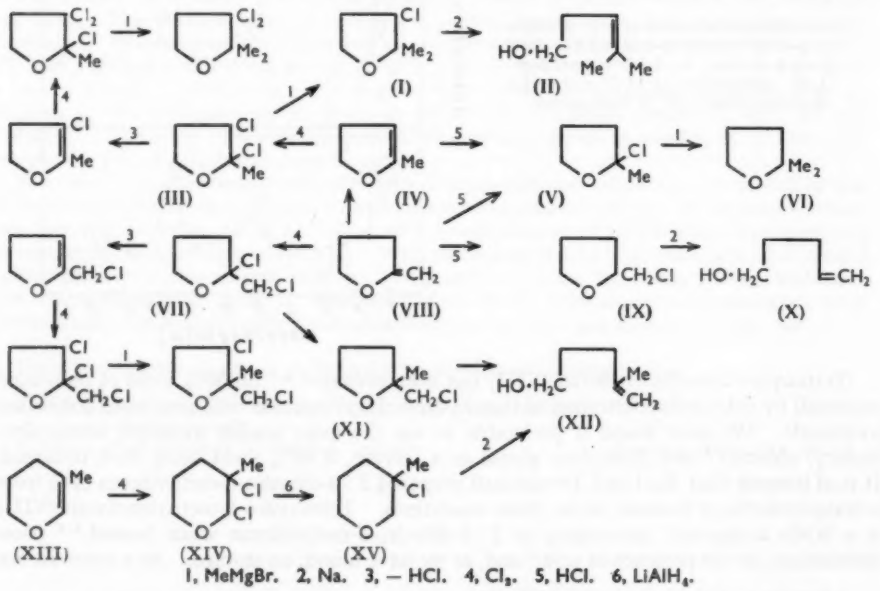
Tetrahydro-2-methylenefuran (VIII) has been prepared [6,7] (in 30% yield of redistilled material) by dehydrohalogenation of tetrahydrofurfuryl bromide with powdered potassium hydroxide. We have found it preferable to use the more readily available tetrahydrofurfuryl chloride [3] and diethylene glycol as a solvent, a 68% yield being then obtained. It is of interest that Paul and Tchelitcheff prepared 2 : 3-dihydro-5-methylfuran (IV) from tetrahydrofurfuryl bromide under these conditions. Tetrahydro-2-methylenefuran (VIII) is a labile compound isomerising to 2 : 3-dihydro-5-methylfuran when heated [7,8] (slow distillation), in the presence of acid,[9] and, as we have found, on storage. As a consequence

[1] Crombie and Harper, *J.*, 1950, 1707, 1714.
[2] Ansell and Selleck, *J.*, 1956, 1238.
[3] Ansell and Brown, *J.*, 1957, 1788.
[4] Brooks and Snyder, *Org. Synth.*, Coll. Vol. III, 1955, p. 698.
[5] Ficini, *Bull. Soc. chim. France*, 1956, **23**, 119.
[6] Paul, *ibid.*, 1933, **53**, 417.
[7] Paul and Tchelitcheff, *ibid.*, 1950, **17**, 520.
[8] Eglinton, Jones, and Whiting, *J.*, 1952, 2873.
[9] Thomas and Wilson, *J. Amer. Chem. Soc.*, 1951, **73**, 4803.

XUM

its preparation must be carried out expeditiously and it must be used immediately. The acid-catalysed conversion of the isomer with the exocyclic double bond to that with the endocyclic double bond is paralleled by that of methylene*cyclo*pentane to methyl*cyclo*pentene [10] and is at variance with the generalisation of Brown, Brewster, and Shechter [11] (which they consider applicable to the tetrahydrofuran ring) that " reactions will proceed in such a manner to favour the formation or retention of an exo double bond in a 5-ring."

In an attempt to avoid, or at least minimise, isomerisation of the methylene compound during its reaction with chlorine, it was added to chlorine at −60° and the reaction mixture immediately added to an excess of methylmagnesium bromide. Distillation gave tetrahydro-2 : 2-dimethylfuran (VI) (2·5%), a middle fraction, from which material giving analyses for chlorotetrahydrodimethylfuran could be isolated, and a higher-boiling dichlorotetrahydrodimethylfuran fraction (13%). Ring scission with sodium of the above middle fraction gave pent-4-en-1-ol (X) (14%), and a mixture (44·5%) of 4-methylpent-3-en-1-ol (II) with some 4-methylpent-4-en-1-ol (XII) [the presence of the latter was identified from the infrared spectrum of the ring-scission product of a purified sample of the chlorotetrahydrodimethylfuran fraction, although absorption at 11 μ may indicate the presence of yet another component (see diagram)]. These compounds are derived from tetrahydrofurfuryl chloride (IX), 3-chlorotetrahydro-2 : 2-dimethylfuran (I), and 2-methyltetrahydrofurfuryl chloride (XI), and together with the isolation of tetrahydro-2 : 2-dimethylfuran (VI) imply the formation in the chlorination step of 2-chlorotetrahydro-2-methylfuran (V), tetrahydrofurfuryl chloride (IX), 2 : 3-dichlorotetrahydro-2-methylfuran (III), and 2-chlorotetrahydrofurfuryl chloride (VII). The formation of the first pair (V and IX) necessitates the addition of hydrogen chloride to tetrahydro-2-methylenefuran (VIII)




1, MeMgBr. 2, Na. 3, − HCl. 4, $Cl_2$. 5, HCl. 6, $LiAlH_4$.

and possibly 2 : 3-dihydro-5-methylfuran (IV); and formation of the latter pair (III and VII) necessitates the addition of chlorine to the same unsaturated compounds. This is illustrated in the annexed scheme, in which the initial product 2-chlorotetrahydrofurfuryl chloride (VII) is considered to eliminate hydrogen chloride which is known to catalyse the

[10] Turner and Garner, *J. Amer. Chem. Soc.*, 1957, **79**, 253.
[11] Brown, Brewster, and Shechter, *ibid.*, 1954, **76**, 467.

conversion of the methylene compound (VIII) into 2 : 3-dihydro-5-methylfuran (IV). The reaction scheme also illustrates the formation of more highly chlorinated products.

In a separate experiment the addition of hydrogen chloride to tetrahydro-2-methylenefuran (VIII), followed by treatment with methylmagnesium bromide, was shown to yield tetrahydro-2 : 2-dimethylfuran (VI) and tetrahydrofurfuryl chloride. The comparable experiment with 2 : 3-dihydro-5-methylfuran (IV) has been reported [7] also to yield tetrahydro-2 : 2-dimethylfuran. We have confirmed this and obtained no indication of the formation of 3-chlorotetrahydro-2-methylfuran.

In order to identify 4-methylpent-4-en-1-ol (XII) among the above reaction products an authentic sample was prepared by the ring scission with sodium of both 3-bromo- and 3-chloro-tetrahydro-3-methylpyran (XV). These were obtained respectively by treatment of 2 : 3-dibromo- and 2 : 3-dichloro-tetrahydro-3-methylpyran (XIV) [from 3 : 4-dihydro-5-methyl-2*H*-pyran [12] (XIII)] with lithium aluminium hydride, which has been shown [3,13] to reduce αβ-dihalogeno-ethers to β-halogeno-ethers.

From the above results it is apparent that, owing to the complexity of the reaction, the chlorination of tetrahydro-2-methylenefuran, followed by treatment with a Grignard reagent and ring scission of the β-halogeno-ethers produced, is not a satisfactory route to structurally homogeneous alkenols.

## Experimental

In distillations marked (S) a 100 × 0·6 cm. spinning-band fractionating column (E. Haage, Mülheim) was used.

*Tetrahydro-2-methylenefuran.*—Tetrahydrofurfuryl chloride [3] (480 g.) was added to a cold solution of potassium hydroxide (448 g.) in diethylene glycol (1 l.). A fast stream of dry nitrogen was passed through the mixture which was gradually warmed to 105—115°; distillation commenced and a fairly vigorous exothermic reaction ensued. After this had subsided the internal temperature was raised to 155°. The distillate, collected over potassium carbonate, separated into two layers. The upper organic layer was removed, dried (powdered KOH), and rapidly distilled to yield tetrahydro-2-methylenefuran (253 g., 75%), b. p. 98—104°, $n_D^{20}$ 1·4490. Distillation (from powdered KOH) through a 25 × 2 cm. Vigreux column gave material (228 g., 68%) of b. p. 101—102°, $n_D^{20}$ 1·4485. Eglinton, Jones, and Whiting [8] record b. p. 100—102°, $n_D^{19}$ 1·4490; Paul and Tchelitcheff [7] record b. p. 98—99°, $n_D^{19}$ 1·4476.

*Reaction of Methylmagnesium Bromide with the Chlorination Products of Tetrahydro-2-methylenefuran.*—Tetrahydro-2-methylenefuran (168 g., 2 moles), dissolved in dry methylene chloride (180 ml.), was added to a solution of chlorine (136 g., 1·9 moles) in the same solvent (250 ml.) maintained at −50°. The resulting cold solution was added to a stirred solution of methylmagnesium bromide [from magnesium 63·2 g. (2·6 g.-atoms) in ether (600 ml.)]. Refluxing of the solvent resulted and a white solid separated. On completion of the addition the mixture was stirred for a further 1 hr. and then poured on crushed ice and ammonium chloride. The organic layer was separated and the aqueous layer extracted with ether. Distillation of the dried ($MgSO_4$) combined extracts through a 40 × 2 cm. helix-packed column gave the following fractions: (*a*) tetrahydro-2 : 2-dimethylfuran (5 g.), b. p. 86—93°, $n_D^{20}$ 1·4100—1·4108 (b. p. 88—92° on redistillation from sodium) (Found: C, 72·25; H, 11·6. Calc. for $C_6H_{12}O$: C, 72·0; H, 12·0%) (Colonge and Garnier [14] record b. p. 93°, $n_D^{19\cdot6}$ 1·4088; Paul and Tchelitcheff [7] record b. p. 91—92°, $n_D^{19\cdot5}$ 1·4262; Yur'ev Kondrat'eva, and Akishin [15] record b. p. 92·2—92·4°, $n_D^{20}$ 1·4045), (*b*) (130 g.), b. p. 142—151°, $n_D^{20}$ 1·4463—1·4510, and (*c*) (44 g.), b. p. 25—55°/0·3 mm., $n_D^{20}$ 1·4630—1·4750, which on redistillation gave a mixture of dichlorotetrahydrodimethylfurans, b. p. 64—65°/4 mm., $n_D^{20}$ 1·4839 (Found: C, 42·5; H, 5·9; Cl, 42·0. Calc. for $C_6H_{10}OCl_2$: C, 41·9; H, 6·0; Cl, 42·6%). Distillation (S) of a portion (12 g.) of fraction (*b*) gave a mixture (4·6 g.) of compounds (XI and I), b. p. 139—143°, $n_D^{20}$ 1·4458 (Found: Cl, 25·9. Calc. for $C_6H_{11}OCl$: 26·4%), and indications of material, b. p. >149°, $n_D^{20}$ >1·4500 (cf. tetrahydrofurfuryl

[12] Ansell and Gadsby, unpublished work.
[13] Crombie, Gold, Harper, and Stokes, *J.*, 1956, 136.
[14] Colonge and Garnier, *Bull. Soc. chim. France*, 1948, **15**, 432.
[15] Yur'ev, Kondrat'eva, and Akishin, *Zhur. obschei Khim.*, 1953, **23**, 1944.

XUM

chloride, b. p. 151—152°, $n_D^{20}$ 1·4550). Ring scission with sodium (as described below) of the remainder (118 g.) gave substantially pure pent-4-en-1-ol (22 g.), b. p. 140—148°, $n_D^{20}$ 1·4327—1·4350. A redistilled (S) sample had b. p. 138—139°, $n_D^{20}$ 1·4290 (Found: C, 69·8; H, 11·6. Calc. for $C_5H_{10}O$: C, 69·65; H, 11·55%); α-naphthylurethane, m. p. and mixed m. p. 62·5—63° (Crombie, Gold, Harper, and Stokes [13] record b. p. 134—137°, $n_D^{20}$ 1·4301, and α-naphthylurethane, m. p. 62°). Hydrogenation in the presence of Adams catalyst gave pentan-1-ol, b. p. 136—138°, $n_D^{20}$ 1·4104 (α-naphthylurethane, m. p. 65—66°) (Huston and Agett [16] record b. p. 135—137°, $n_D^{20}$ 1·4110, and α-naphthylurethane, m. p. 65·5°) together with a mixture (81 g.), b. p. 153—156°, $n_D^{20}$ 1·4427—1·4444, of 4-methylpent-3-en-1-ol and 4-methylpent-4-en-1-ol (identified from infrared spectrum; for preparation see below) which gave the *α-naphthylurethane* of the former, m. p. and mixed m. p. 85—86° (Found: N, 5·3. $C_{17}H_{19}O_2N$ requires N, 5·2%). Ansell and Brown [3] record b. p. 157—158°, $n_D^{19}$ 1·4452, for 4-methylpent-3-en-1-ol. For constants of 4-methylpent-4-en-1-ol see below. The infrared spectrum of the mixture of isomeric alcohols obtained from ring scission of the redistilled fraction (free from tetrahydrofurfuryl chloride) was determined (see diagram).

Essentially the same results were obtained when chlorine was replaced by bromine, but the intermediates were less stable.

*Addition of Hydrogen Chloride to Tetrahydro-2-methylenefuran and 2 : 3-Dihydro-5-methylfuran.*—Dry hydrogen chloride (32 g., 0·88 mole) was passed into a solution of tetrahydro-2-methylenefuran (74 g.) in ether (200 ml.) at −60° to −65° and the resulting cold solution added to a stirred solution of methylmagnesium bromide (from magnesium, 31 g.) in ether (300 ml.) so that gentle refluxing was maintained. After being stirred for a further 1 hr. the mixture was worked up as after addition of chlorine. Distillation gave tetrahydro-2 : 2-dimethylfuran (46 g., 52%), b. p. 92°, $n_D^{20}$ 1·4094, and, after a small (*ca.* 1 g.) intermediate cut, tetrahydrofurfuryl chloride (13 g., 12%), b. p. 147—153°, $n_D^{20}$ 1·4548—1·4552. Ring scission of the last chloride gave pent-4-en-1-ol, b. p. 136—137° (α-naphthylurethane, m. p. 62°) (cf. above).

In a similar experiment with 2 : 3-dihydro-5-methylfuran, tetrahydro-2 : 2-dimethylfuran, b. p. 92°, $n_D^{20}$ 1·4102, was obtained together with material of high b. p. No evidence of an appreciable quantity of 3-chlorotetrahydro-2-methylfuran was obtained (cf. Paul and Tchelitcheff [7]).

*3-Halogenotetrahydro-3-methylpyran.*—A solution of 2 : 3-dihalogenotetrahydro-3-methylpyran [11] [from 3 : 4-dihydro-5-methyl-2*H*-pyran (60 g., 0·6 mole)] in ether (120 ml.) was added to a stirred suspension of lithium aluminium hydride (8·5 g. of 85% purity, equiv. to 0·18 mole) in ether (300 ml.) so that vigorous refluxing was maintained. The mixture was boiled and stirred for a further 1 hr. and then decomposed (caution; cf. ref. 17) by the addition of wet ether and then water. The ethereal solution was decanted from the residual solid which was washed with ether by decantation. The combined extracts were washed with 10% sodium hydroxide solution, then with water, and dried ($MgSO_4$). Distillation gave in one case *3-bromotetrahydro-3-methylpyran* (71 g., 61%), b. p. 67—72°/20 mm., $n_D^{20}$ 1·4902—1·4904 (an analytical sample had b. p. 71°/20 mm., $n_D^{20}$ 1·4903) (Found: C, 40·6; H, 6·4; Br, 44·3. $C_6H_{11}OBr$ requires C, 40·3; H, 6·2; Br, 44·7%), and in the other *3-chlorotetrahydro-3-methylpyran* (55·5 g., 70%), b. p. 66—69°/37 mm., $n_D^{20}$ 1·4553 (an analytical sample had b. p. 68°/36 mm., $n_D^{20}$ 1·4577) (Found: C, 53·9; H, 8·3; Cl, 25·9. $C_6H_{11}OCl$ requires C, 53·6; H, 8·2; Cl, 26·4%).

*4-Methylpent-4-en-1-ol.*—A little 3-halogenotetrahydro-3-methylpyran was added to a suspension of powdered sodium (19 g.) in ether (50 ml.), and the mixture stirred until reaction commenced as indicated by boiling of the ether and appearance of a blue colour on the surface of the sodium. Ether (100 ml.) was added, followed by the remainder of the 3-halogenotetrahydro-3-methylpyran (0·4 mole in all) in ether (100 ml.), so as to maintain vigorous boiling. After being stirred for a further 2 hr., the mixture was decomposed by the cautious addition of water. The ether layer was separated and the aqueous layer extracted with ether (2 × 100 ml.). Distillation of the dried ($MgSO_4$) combined extracts gave *4-methylpent-4-en-1-ol* (65% from 3-bromo and 85% from 3-chloro), b. p. 64—68°/20 mm., $n_D^{20}$ 1·4382. A redistilled (S) sample had b. p. 67·5—68°/19 mm., $n_D^{20}$ 1·4372 (Found: C, 71·7; H, 12·2. $C_6H_{12}O$ requires C, 71·95; H, 12·1%). The derived *α-naphthylurethane* [needles from light petroleum (b. p. 40—60°)] had m. p. 52—53° (Found: C, 75·5; H, 7·4; N, 5·15. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1; N, 5·2%).

[16] Huston and Agett, *J. Org. Chem.*, 1941, **6**, 123.
[17] Bessant, *Chem. and Ind.*, 1957, 432.

XUM

The authors are indebted to the Ministry of Education for a grant (to D. A. T.), to the University of London Central Research Fund for financial assistance.

QUEEN MARY COLLEGE, UNIVERSITY OF LONDON,
MILE END ROAD, LONDON, E.1. [*Received, October 10th*, 1957.]

---

## 229. *Reduced Cyclic Compounds. Part III.* The Preparation and Cyclodehydration of Some Unsaturated Tertiary Alcohols.*

By M. F. ANSELL and (the late) M. E. SELLECK.

Preparations are reported of 2-methyloct-6-en-2-ol, 2-methyldodeca-6 : 10-dien-2-ol, and 2-methylhexadeca-6 : 10 : 14-trien-2-ol. These have been subjected to cyclodehydration with phosphoric acid.

IN Part I of this series [1] the preparations of two ω-phenyl unsaturated tertiary alcohols were reported and it was stated that the same synthetical route, namely consecutive chain extensions with 1 : 2-dichlorotetrahydro-furan or -pyran, was applicable to completely aliphatic compounds. This has now been substantiated by the preparation of the unsaturated tertiary alcohols (I), (VII), and (XIII). The cyclodehydration of these alcohols to the reduced monocyclic, bicyclic and tricyclic compounds (II), (VIII), and (XIV) is reported.

*trans*-2-Methyloct-6-en-1-ol (I) was prepared from *trans*-hex-4-en-1-ol,[2] by reaction of the Grignard reagent from the derived bromide with acetone. Treatment of this alcohol with hot 85% phosphoric acid (cf. ref. 3) gave a 46% yield of substantially monocyclic material (from analysis and catalytic hydrogenation). Of the products to be expected, on the basis of the accepted mechanism [4, 5] for such reactions, namely, 2 : 3 : 3- (II) and 3 : 4 : 4-trimethyl*cyclo*hexene (III), the former has been previously prepared [6, 7] and was found to be a product of this cyclisation. It was identified by the preparation of its nitrosochloride and by ozonolysis to 5 : 5-dimethyl-6-oxoheptanoic acid (isolated as the semicarbazone). This conclusion is supported by the infrared spectrum of the product which had bands at 5·97 and 12·50 μ (trisubstituted double bond [5]); bands due to *cis*-CH=CH and C=$CH_2$ were not detectable and therefore 3 : 4 : 4-trimethyl*cyclo*hexene must be the predominant product of the cyclisation.

The cyclisation product may contain a little 2-methylocta-2 : 6-diene obtained by dehydration of the alcohol (I), as in one ozonolysis experiment a small amount of succinic acid was isolated, possibly together with a small amount of 3 : 4 : 4-trimethyl*cyclo*hexene. This result is similar to that of Openlander and Day [5] who showed that, contrary to earlier reports,[8] cyclodehydration of 3 : 7-dimethyloct-6-en-3-ol (IV) yields predominantly 1 : 2 : 3 : 3-tetramethyl*cyclo*hexene together with a little 2 : 3 : 4 : 4-tetramethyl*cyclo*hexene.

2-Methyldodeca-6 : 10-dien-2-ol (VII), the precursor of a bicyclic system, was then prepared. 3-Chlorotetrahydro-2-(pent-3-enyl)pyran (V) obtained from 5-bromopent-2-ene [2] and 2 : 3-dichlorotetrahydropyran, gave, on treatment with sodium, deca-4 : 8-dien-1-ol (VI). Conversion of the latter into 2-methyldodeca-6 : 10-dien-2-ol (VII) was accomplished by reaction of acetone with the Grignard reagent derived from the corresponding bromide. The tertiary alcohol (VII) was not stereochemically pure, being from

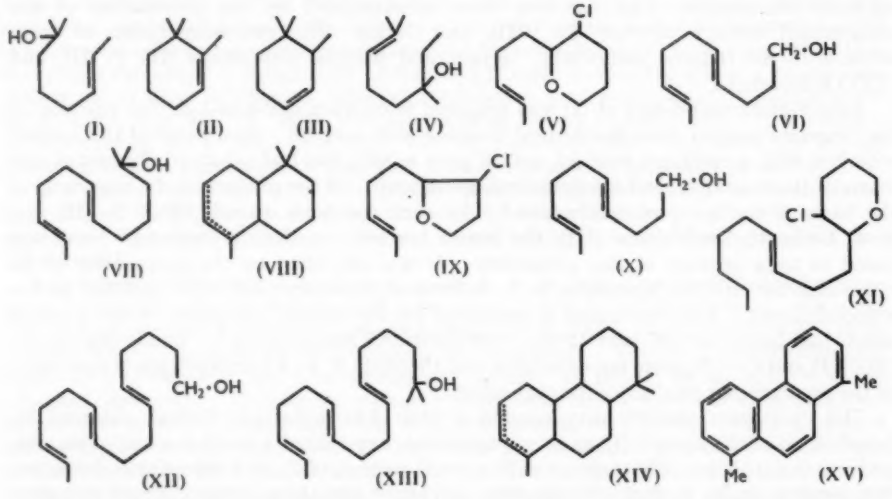
* Part II, *J.*, 1956, 4518.

[1] Ansell and Selleck, *J.*, 1956, 1238.
[2] Crombie and Harper, *J.*, 1950, (*a*) 1707, (*b*) 1714.
[3] Linstead, *J.*, 1936, 474.
[4] Stork and Burgstahler, *J. Amer. Chem. Soc.*, 1955, **77**, 5068.
[5] Openlander and Day, *J. Org. Chem.*, 1956, **21**, 961.
[6] Auwers and Lange, *Annalen*, 1915, **409**, 174.
[7] Godchot and Bedos, *Comp. rend.*, 1925, **181**, 920.
[8] Dupont and Dulou, *ibid.*, 1935, **201**, 219; Escourrou, *Bull. Soc. chim. France*, 1926, **39**, 1126, 1460.

XUM

its method of preparation a mixture of 6 : 7-*trans*-10 : 11-*cis*-isomer and the all-*trans*-isomer, with the latter predominating. Treatment of the tertiary alcohol (VII) with hot 85% phosphoric acid gave a mixture of octahydro-1 : 1 : 5-trimethylnaphthalenes (VIII) in which the position of the double bond is uncertain.

For the preparation of a phenanthrene derivative 2-methylhexadeca-6 : 10 : 14-trien-2-ol (XIII) was prepared. Ring scission of 3-chlorotetrahydro-2-(pent-3-enyl)furan (IX), from 5-bromopent-2-ene and 2 : 3-dichlorotetrahydrofuran, gave nona-3 : 7-dien-1-ol (X). Application of the chain-extension procedure with 2 : 3-dichlorotetrahydropyran gave the chloride (XI) and thence tetradeca-4 : 8 : 12-trien-1-ol (XII) which was converted in two stages into the required tertiary alcohol (XIII). This alcohol is not stereochemically pure: the 6 : 7-double bond is *trans*, but the 10 : 11- and 14 : 15-double bonds arise from the non-stereospecific ring scission of furan derivatives. Treatment of the alcohol (XIII) with hot 85% phosphoric acid gave a mixture of dodecahydro-1 : 1 : 8-trimethylphenanthrenes (XIV) in which the position of the double bond is uncertain. The structure of the product was confirmed by hydrogenation (one double bond) and dehydrogenation to 1 : 8-dimethylphenanthrene (XV).




The above method for the conversion of long-chain unsaturated alcohols into reduced cyclic systems is limited by the uncertainty as to the final position of the double bond, and also, in the polycyclic cases, the stereochemistry of the product.

## Experimental

trans-6-*Bromohex*-2-*ene*.—This bromide, prepared as previously described,[1] had b. p. 42°/12 mm., $n_D^{20}$ 1·4690 (a redistilled fraction had $n_D^{20}$ 1·4695) (Found: C, 44·1; H, 6·95; Br, 48·95. Calc. for $C_6H_{11}Br$: C, 44·2; H, 6·75; Br, 49·1%). It gave a *thiuronium picrate*, yellow plates (from ethanol), m. p. 152—153° (Found: N, 18·1. $C_{13}H_{17}N_5O_7S$ requires N, 18·1%).

trans-2-*Methyloct*-6-*en*-2-*ol*.—The Grignard reagent from the above bromide (0·6 mole) was treated with acetone as in the preparation of 2-methyl-9-phenylnon-6-en-2-ol.[10] Distillation gave 2-*methyloct*-6-*en*-2-*ol* (69%), b. p. 82—83°/14 mm., $n_D^{20}$ 1·4444 (Found: C, 76·5; H, 12·9.

[9] Ansell and Brown, *J.*, 1957, 1788.
[10] Crossley and Renouf, *J.*, 1911, **99**, 1111.

$C_9H_{18}O$ requires C, 76·1; H, 12·7%). In one preparation dehydration occurred during the distillation, to yield *2-methylhexa-2 : 6-diene*, b. p. 144°, $n_D^{20}$ 1·4384 (Found: C, 87·0; H, 13·1. $C_9H_{16}$ requires C, 87·1; H, 12·9%).

*Cyclodehydration of* trans-*2-Methyloct-6-en-2-ol.*—A stirred mixture of the above alcohol (30 g.) and 85% phosphoric acid (140 ml.) was heated at 100° for 1 hr., cooled, poured into water, and extracted with ether. The extract was washed with water, then sodium hydrogen carbonate solution, and dried ($K_2CO_3$). After removal of the ether, the residue was refluxed over sodium and distilled. The 2 : 3 : 3-trimethyl*cyclo*hexene fraction (12 g., 46%), b. p. 143—146°, $n_D^{20}$ 1·4502—1·4540 was collected (Found: C, 87·1; H, 13·2. Calc. for $C_9H_{16}$: C, 87·1; H, 12·9%). Auwers and Lange [6] record b. p. 146·2—147·2°, $n_D^{20·4}$ 1·456; Godchot and Bedos [7] record b. p. 144—146°, $n_D^{14}$ 1·4590. Hydrogen uptake at atmospheric pressure in presence of Adams catalyst was equivalent to 1·1 double bonds.

A mixture of this hydrocarbon (1 g.), glacial acetic acid (1 ml.), and pentyl nitrite (2 ml.) was cooled in ice, and a mixture of 10N-hydrochloric acid (2 ml.) and glacial acetic acid (0·5 ml.) added slowly with shaking. After 3 hr. at 0°, with intermittent shaking, the precipitated nitrosochloride (0·1 g.) was filtered off, and after being washed thoroughly with alcohol and acetone and dried, had m. p. 133—134° (rapid heating). Auwers and Lange [6] record the nitrosochloride of 2 : 3 : 3-trimethyl*cyclo*hexene as having m. p. 133—134° (rapid heating).

*Ozonolysis.* A solution of the cyclisation product (2 g.) in acetic acid (5 ml.) was treated with ozonised air for 12 hr. Water (5 ml.) and 30% hydrogen peroxide (3 ml.) were then added and the solution was boiled for 30 min. The cold solution was extracted (continuously) with ether, and the ethereal solution extracted with 10% sodium hydroxide solution. After being acidified the aqueous solution was extracted with ether. The residue obtained on evaporation of the dried ($MgSO_4$) extract was boiled for 30 min. with a solution of semicarbazide hydrochloride (0·6 g.) and pyridine (0·6 ml.) in alcohol (2 ml.). The residue obtained on evaporation of this solution partly solidified and was filtered off, washed with a little alcohol, and recrystallised from alcohol, to yield the semicarbazone of 5 : 5-dimethyl-6-oxoheptanoic acid, m. p. 169—171° (Found: N, 18·2. Calc. for $C_{10}H_{19}O_3N$: N, 18·3%). Auwers and Lange [6] record m. p. 167—169°. Crossley and Renouf [10] record m. p. 169°.

2 : 3 : 3-*Trimethyl*cyclo*hexane*-1 : 2-*diol.*—The cyclisation product (12·4 g.) was added to a stirred mixture of 100% formic acid (80 ml.) and 30% hydrogen peroxide (12 g.). The temperature of the mixture rose to 50°, and was then kept at 40° for 2 hr., water (200 ml.) added, and the whole was extracted with ether. After being washed with water the extract was evaporated and the residue boiled with 10% sodium hydroxide solution for 30 min., cooled, neutralised with hydrochloric acid, and extracted with ether. The extract was washed with water and sodium hydrogen carbonate solution and dried ($MgSO_4$). Distillation gave the *glycol* (2 g.), b. p. 110—120°/7—8 mm., which solidified and crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 115—116° (Found: C, 68·3; H, 11·6. $C_9H_{18}O$ requires C, 68·4; H, 11·4%).

It was not possible to repeat this reaction.

3-*Chlorotetrahydro*-2-(*pent*-3-*enyl*)*pyran.*—A solution of 2 : 3-dichlorotetrahydropyran [2a] (from 57 g. of dihydropyran) in ether (100 ml.) was treated with the Grignard reagent from 5-bromopent-2-ene [2b] (149 g.) as in the preparation of 3-chlorotetrahydrophenethylfuran.[1] Distillation gave 3-*chlorotetrahydro*-2-(*pent*-3-*enyl*)*pyran* (63 g., 43·5%), b. p. 123—140°/19 mm., $n_D^{20}$ 1·4758—1·4793 (Found: C, 63·6; H, 9·2. $C_{10}H_{17}OCl$ requires C, 63·7; H, 9·0%).

*Deca*-4 : 8-*dien*-1-*ol.*—3-Chlorotetrahydro-2-(pent-4-enyl)pyran was subjected to ring scission with sodium as in the preparation of 7-phenylhept-4-en-1-ol.[1] Distillation gave *deca*-4 : 8-*dien*-1-*ol* (78%) b. p. 124—126°/17 mm., $n_D^{20}$ 1·4654 (Found: C, 77·8; H, 11·8. $C_{10}H_{18}O$ requires C, 77·9; H, 11·7%). The derived 3 : 5-*dinitrobenzoate*, plates from light petroleum (b. p. <40°), had m. p. 43—45° (Found: C, 58·3; H, 5·9; N, 8·2. $C_{17}H_{20}O_6N_2$ requires C, 58·6; H, 5·75; N, 8·05%).

10-*Bromodeca*-2 : 6-*diene.*—A mixture of deca-4 : 8-dien-1-ol (40 g.) and pyridine (6 ml.) was added dropwise with stirring to phosphorus tribromide (28 g.) with ice-cooling. The subsequent procedure was as for 6-bromohex-2-ene.[9] The final distillation gave 10-*bromodeca*-2 : 6-*diene* (36 g., 64%), b. p. 114—116°/10 mm., $n_D^{20}$ 1·4845 (Found: C, 55·7; H, 8·0. $C_{10}H_{17}Br$ requires C, 55·3; H, 7·8%); the *thiuronium picrate* had m. p. 130—131° (from ethanol) (Found: N, 15·7. $C_{17}H_{23}O_7N_7S$ requires N, 15·9%).

2-*Methyldodeca*-6 : 10-*dien*-2-*ol.*—This alcohol was prepared from the Grignard reagent of 10-bromodeca-2 : 6-diene and acetone as in the preparation of 2-methyl-9-phenylnon-6-en-2-ol.[1]

Distillation gave *2-methyldodeca-6 : 10-dien-2-ol* (29%), b. p. 131—135°/14 mm., $n_D^{20}$ 1·4640 (Found: C, 79·3; H, 12·2. $C_{13}H_{24}O$ requires C, 79·6; H, 12·2%).

*Cyclodehydration of 2-Methyldodeca-6 : 10-dien-2-ol.*—A stirred mixture of the alcohol (8 g.) and 85% phosphoric acid (50 ml.) was heated at 140° for 1 hr. The subsequent procedure was as for the cyclodehydration of 2-methyloct-6-en-2-ol. Distillation gave octahydro-1 : 1 : 5-trimethylnaphthalene (4 g., 55%), b. p. 100—106°/15 mm., $n_D^{20}$ 1·4803—1·4810 (Found: C, 87·4; H, 12·6. $C_{13}H_{22}$ requires C, 87·6; H, 12·4%). Hydrogen uptake at atmospheric pressure in presence of Adams catalyst was equivalent to 1·01 double bonds.

*3-Chlorotetrahydro-2-(pent-3-enyl)furan.*—2 : 3-Dichlorotetrahydrofuran (0·62 mole) was coupled with the Grignard reagent prepared from 5-bromopent-2-ene [20] (1 mole) as in the preparation of 3-chlorotetrahydro-2-phenethylfuran.[1] Distillation gave, after elimination of low-boiling material (pent-3-ene), *3-chlorotetrahydro-2-(pent-3-enyl)furan* (61·5%), b. p. 90—105°/9—11 mm. $n_D^{20}$ 1·4705—1·4745 (Found: C, 61·8; H, 8·8; Cl, 20·0. $C_9H_{15}OCl$ requires C, 62·1; H, 8·6; Cl, 20·4%).

*Nona-3 : 7-dien-1-ol.*—Ring scission of 3-chlorotetrahydro-2-(pent-3-enyl)furan with sodium was effected as for the pyran. Distillation gave *nona-3 : 7-dien-1-ol* (81%), b. p. 98—100°/11 mm., $n_D^{20}$ 1·4657—1·4663 (Found: C, 77·4; H, 11·6. $C_9H_{16}O$ requires C, 77·1; H, 11·4%).

*9-Bromonona-2 : 6-diene.*—A mixture of nona-3 : 7-dien-1-ol (40 g.) and pyridine (3 ml.) was added dropwise with stirring to phosphorus tribromide with ice cooling. The subsequent procedure was as for 6-bromohex-2-ene. The final distillation gave *9-bromonona-2 : 6-diene* (33 g., 56·5%), b. p. 86—88°/7—8 mm., $n_D^{20}$ 1·4872 (Found: C, 53·9; H, 7·4; Br, 39·4. $C_9H_{15}Br$ requires C, 53·2; H, 7·4; Br, 39·4%).

*9-Chlorononа-2 : 6-diene.*—Pure thionyl chloride (225 g.) was added slowly to a stirred mixture of nona-3 : 7-dien-1-ol (212 g.) and pyridine (0·75 ml.), the internal temperature being kept below 20°. The mixture was then slowly heated to boiling and maintained under reflux for 2 hr. It was then cooled, 100% formic acid (20 g.) added slowly, and then the whole was heated under reflux for 30 min., cooled, and poured into saturated brine. The organic layer was separated and the aqueous layer extracted with ether. The combined organic material was washed with 10% sodium hydrogen carbonate solution and water and dried ($MgSO_4$). Distillation gave, after removal of the solvent, *9-chlorononа-2 : 6-diene* (192 g., 79·5%), b. p. 86—88°/14 mm., $n_D^{20}$ 1·4668 (Found: C, 68·3; H, 9·5; Cl, 22·7. $C_9H_{15}Cl$ requires C, 68·1; H, 9·5; Cl, 22·4%).

*Tetradeca-4 : 8 : 12-trien-1-ol.*—The Grignard reagent from 9-chlorononа-2 : 6-diene (1·15 moles) was coupled with 2 : 3-dichlorotetrahydropyran (from 76 g., 0·9 mole, of 2 : 3-dihydropyran) as in the preparation of 3-chlorotetrahydro-2-phenethylpyran.[1] Distillation gave crude 3-chlorotetrahydro-2-(nona-3 : 7-dienyl)pyran (160 g.), b. p. 75—120°/$10^{-3}$ mm., which was not further purified but was subjected to ring scission with sodium as for 3-chlorotetrahydro-2-phenethylpyran.[1] Distillation gave *tetradeca-4 : 8 : 12-trien-1-ol* (33·5% calc. on chloride), b. p. 100—104°/$10^{-3}$ mm., $n_D^{20}$ 1·4797—1·4801 (Found: C, 81·1; H, 11·5. $C_{14}H_{24}O$ requires C, 80·8; H, 11·5%).

*14-Chlorotetradeca-2 : 6 : 10-triene.*—The preceding alcohol (76 g.) was treated with thionyl chloride (66 g.) and pyridine (0·2 ml.) and then formic acid (16 g.) as in the preparation of 9-chlorononа-2 : 6-diene. Distillation gave *14-chlorotetradeca-2 : 6 : 10-triene* (57 g., 68·5%), b. p. 98—102°/5 × $10^{-3}$ mm., $n_D^{20}$ 1·4785—1·4795 (Found: C, 73·9; H, 10·4; Cl, 15·1. $C_{14}H_{23}Cl$ requires C, 74·2; H, 10·15; Cl, 15·7%).

*2-Methylhexadeca-6 : 10 : 14-trien-2-ol.*—The Grignard reagent from 14-chlorotetradeca-2 : 6 : 10-triene (0·24 mole) was treated with acetone as in the preparation of 2-methyl-9-phenylnon-6-en-2-ol.[10] Distillation gave *2-methylhexadeca-6 : 10 : 14-trien-2-ol* (33 g., 49·5%), b. p. 108—110°/$10^{-3}$ mm., $n_D^{20}$ 1·4763—1·4768 (Found: C, 81·5; H, 12·2. $C_{17}H_{30}O$ requires C, 81·6; H, 12·0%).

*Cyclodehydration of 2-Methylhexadeca-6 : 10 : 14-trien-2-ol.*—A stirred mixture of preceding alcohol (31 g.) and 85% phosphoric acid (200 ml.) was heated at 140° for 1 hr. and then worked up as in the preceding cyclisations. Distillation from sodium gave a mixture of 1 : 1 : 8-trimethyldodecahydrophenanthrenes (21 g., 72·5%), b. p. 91—102°/$10^{-3}$ mm. (Found: C, 87·7; H, 12·45. $C_{17}H_{28}$ requires C, 87·9; H, 12·1%). This product absorbed hydrogen equivalent to one double bond in presence of Adams catalyst at atmospheric pressure.

*Dehydrogenation.* A mixture of the hydrocarbon (0·5 g.) and selenium (2·5 g.) was heated in

a sealed tube at 360° for 24 hr. The product was extracted with chloroform and filtered. The solid left on evaporation of the chloroform was crystallised from benzene, sublimed, and recrystallised from acetic acid. It had m. p. 185—188° not depressed on admixture with an authentic specimen [11] (m. p. 187—190°).

The authors are indebted to Dr. R. K. Callow for determination of infrared spectra, to Dr. P. A. Robins for a sample of 1 : 8-dimethylphenanthrene, and to the D.S.I.R. for an award (to M. E. S.).

QUEEN MARY COLLEGE, UNIVERSITY OF LONDON,
MILE END ROAD, LONDON, E.1. [*Received, October 10th*, 1957.]

[11] Robins and Walker, *J.*, 1952, 1615.

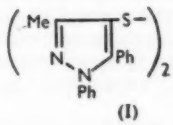
---

## 230. *Fission of Di-(3-methyl-1 : 5-diphenyl-4-pyrazolyl) Disulphide by Chlorine.*

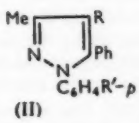
By W. J. BARRY.

Treatment of di-(3-methyl-1 : 5-diphenyl-4-pyrazolyl) disulphide (I) with chlorine in anhydrous conditions results in desulphurisation, accompanied by nuclear chlorination. Chlorination in aqueous medium gives the thiolsulphonate (III).

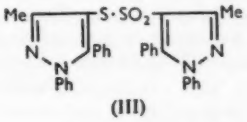
THE following investigation was undertaken, because preliminary experiments on the chlorination of di-(3-methyl-1 : 5-diphenyl-4-pyrazolyl) disulphide [1] (I) indicated some unusual features. The primary product from the action of one mol. of chlorine in carbon tetrachloride on the disulphide (I) was a viscous oil which reacted vigorously with water and with bases such as ammonia and aniline. Since the original disulphide was recovered from all these reactions, the oil could not be identified as the sulphenyl chloride [2] (II; R = SCl, R′ = H).




(I)




(II)




(III)

However, addition of further chlorine to the primary product resulted in desulphurisation, and the formation of 4-chloro-3-methyl-1 : 5-diphenylpyrazole (II; R = Cl, R′ = H), and 4-chloro-1-*p*-chlorophenyl-3-methyl-5-phenylpyrazole (II; R = R′ = Cl). This type of bilateral fission between sulphur atoms and aromatic carbon in a disulphide appears to be new, although nuclear chlorination accompanying the fission of a C–S bond is known to occur with certain sulphides.[3,4,5]

By using a standard solution of chlorine, the extent of nuclear chlorination could be controlled to give either of the two chloropyrazoles as the main product. The monochloro-compound was also synthesised from 2-chloro-1-phenylbutane-1 : 3-dione [6] and phenylhydrazine, as well as by treatment of 3-methyl-1 : 5-diphenylpyrazole (II; R = R′ = H) with the calculated amount of chlorine solution. Attempts to prepare the

[1] Barry, Finar, and Simmonds, *J.*, 1956, 4974.
[2] Kharasch, Potempa, and Wehrmeister, *Chem. Rev.*, 1946, **39**, 278 *et seq.*
[3] Douglass, Brower, and Martin, *J. Amer. Chem. Soc.*, 1952, **74**, 5770.
[4] Baker, Dodson, and Riegel, *ibid.*, 1946, **68**, 2638.
[5] Kwart and Miller, *ibid.*, 1956, **78**, 5008.
[6] Morgan, Drew, and Barker, *J.*, 1922, 2456.

XUM

dichloro-compound (II; R = R′ = Cl) by cold chlorination of 3-methyl- or 4-chloro-3-methyl-1 : 5-diphenylpyrazole failed, perhaps owing to the absence of an effective catalyst for nuclear chlorination such as may be formed during the decomposition of the disulphide (I). Chlorination of certain disulphides gives rise to unstable compounds which might act in this way (*e.g.*, phenylsulphur trichloride from diphenyl disulphide [4]). The required dichloro-compound (II; R = R′ = Cl) was readily synthesised, however, by condensing benzoylacetone with *p*-chlorophenylhydrazine to give 1-*p*-chlorophenyl-3-methyl-1 : 5-diphenylpyrazole (II; R = H, R′ = Cl), and then chlorinating the pyrazole nucleus. The fact that the pyrazole from 2-chloro-1-phenylbutane-1 : 3-dione and *p*-nitrophenylhydrazine gives the same dichloro-compound (II; R = R′ = Cl) when the nitro-group is replaced by chlorine shows it to be 4-chloro-3-methyl-1-*p*-nitrophenyl-5-phenylpyrazole (II; R = Cl, R′ = $NO_2$) so that the alternative structure given in the literature may now be disregarded.[6,7] It is clear from the structural relation between the pyrazoles from 2-chloro-1-phenylbutane-1 : 3-dione and 3-methyl-1 : 5-diphenylpyrazole that the chlorine substituent, in common with others in the methylene group of benzoylacetone, does not alter the normal mode of ring closure with phenyl- and *p*-nitrophenyl-hydrazine.[8]

Treatment of the disulphide (I) with chlorine in aqueous acetic acid did not give the expected 4-chlorosulphonyl-3-methyl-1 : 5-diphenylpyrazole [9] (II; R = $SO_2Cl$, R′ = H) but, instead, 3-methyl-1 : 5-diphenyl-4-pyrazolyl 3-methyl-1 : 5-diphenylpyrazole-4-thiolsulphonate (III). This thiolsulphonate was also obtained by controlled oxidation of the disulphide (I) with hydrogen peroxide in acetic acid.[10] Reduction of the thiolsulphonate with zinc in acid solution gave the corresponding thiol (II; R = SH, R′ = H), characterised by conversion into the disulphide (I) with ferric chloride. The thiolsulphonate structure of (III) was confirmed by the presence of characteristic infrared bands [11] at 1333 and 1140 cm.$^{-1}$.

## Experimental

*4-Chloro-3-methyl-1 : 5-diphenylpyrazole.*—(a) *From di-(3-methyl-1 : 5-diphenyl-4-pyrazolyl) disulphide.* The disulphide (5·3 g., 0·01 mol.), suspended in dry carbon tetrachloride (60 c.c.) containing chlorine (2·13 g., 0·03 mol.), gave, after storage for 40 min. at 20° and evaporation of the solvent under reduced pressure, a yellow oil (5·5 g.). The solvent, collected at −80° had the odour and reactions characteristic of sulphur dichloride. The residual oil gave crystals of *4-chloro-3-methyl-1 : 5-diphenylpyrazole* (3 g., 56%), m. p. 50° (from methanol), rising to 67—69° on storage, the two forms giving identical infrared spectra in $CCl_4$ (Found: C, 71·8; H, 4·5; N, 10·7; Cl, 12·9. $C_{16}H_{13}N_2Cl$ requires C, 71·5; H, 4·8; N, 10·4; Cl, 13·2%). Some of the disulphide (0·65 g.), m. p. and mixed m. p. 202°, was recovered.

(b) *From 3-methyl-1 : 5-diphenylpyrazole.* 3-Methyl-1 : 5-diphenylpyrazole (8 g., 0·034 mol.), treated with chlorine in dry carbon tetrachloride (2·4 g., 0·034 mol.) at 20°, gave a precipitate of the hydrochloride of the monochloro-derivative. On removal of the solvent at 100° under reduced pressure, the original precipitate redissolved and a yellowish oil remained. After several days in methanol solution (75 c.c.), this residue gave colourless crystals (8 g., 87%), m. p. 67—68° alone or mixed with 4-chloro-3-methyl-1 : 5-diphenylpyrazole prepared as in (a).

(c) *From 2-chloro-1-phenylbutane-1 : 3-dione.* The diketone (1·96 g., 0·01 mol.) was slowly mixed with phenylhydrazine (1·1 g., 0·01 mol.) in ethanol (cooling). After 3 hr. at 100° and cooling to −80°, crystals of 4-chloro-3-methyl-1 : 5-diphenylpyrazole (1 g., 37%) separated from the dark oily mixture. These had m. p. 50° (from methanol), rising to 67—69°, alone or mixed with the previous preparations.

*4-Chloro-1-p-chlorophenyl-3-methyl-5-phenylpyrazole.*—(a) *From the disulphide.* A solution of the disulphide (5·3 g., 0·01 mol.) in dry carbon tetrachloride (100 c.c.) containing chlorine

[7] Macbeth, *J.*, 1923, 1128.
[8] Elderfield, "Heterocyclic Compounds," J. Wiley, New York, Vol. V, p. 49.
[9] Fromm, *Z. angew. Chem.*, 1911, **24**, 1125.
[10] Hinsberg, *Ber.*, 1908, **41**, 2836; 1909, **42**, 1278.
[11] Cf. Cymerman and Willis, *J.*, 1951, 1332.

(3·55 g., 0·05 mol.), gave, after 24 hr. at room temperature, colourless crystals (0·75 g.) of 4-chloro-3-methyl-1 : 5-diphenylpyrazole, m. p. 67° (from methanol) alone or mixed with previous specimens, and *4-chloro*-1-p-*chlorophenyl*-3-*methyl*-5-*phenylpyrazole* (2·2 g.), m. p. 112° (from methanol) (Found: C, 63·7; H, 3·8; N, 9·7; Cl, 22·9. $C_{16}H_{12}N_2Cl_2$ requires C, 63·4; H, 3·96; N, 9·2; Cl, 23·3%).

(b) *From benzoylacetone and* p-*chlorophenylhydrazine.* Equimolecular proportions of benzoylacetone and *p*-chlorophenylhydrazine (prepared by Hunsberger's method [12] for substituted arylhydrazines), when boiled in ethanol for 2 hr., gave 1-p-*chlorophenyl*-3-*methyl*-5-*phenylpyrazole*, m. p. 105° (from ethanol) (Found: Cl, 13·2. $C_{16}H_{13}N_2Cl$ requires Cl, 13·2%). Chlorination of this compound in carbon tetrachloride gave 4-chloro-1-*p*-chlorophenyl-3-methyl-5-phenylpyrazole, m. p. 111° (from methanol) undepressed on admixture with a specimen prepared from the disulphide.

(c) *From 4-chloro-3-methyl*-1-p-*nitrophenyl*-5-*phenylpyrazole.* The above compound (1 g.) was heated in ethanol (25 c.c.) with palladised charcoal (0·15 g.) and hydrazine hydrate (2 c.c.). 1-p-*Aminophenyl*-3-*methyl*-5-*phenylpyrazole* crystallised on cooling and had m. p. 181—182° (from ethanol) (Found: C, 67·7; H, 4·9; Cl, 12·6; N, 15·0. $C_{16}H_{14}N_3Cl$ requires C, 67·7; H, 4·9; Cl, 12·5; N, 14·8%). The amine (3 g.) was diazotised at 40°, and the solution run immediately into boiling concentrated hydrochloric acid (25 c.c.) containing cuprous chloride (3 g.). After 0·5 hr. at 100°, a brown oil remained; this product, crystallised from methanol, had m. p. 111—112° alone or mixed with previous specimens of 4-chloro-1-*p*-chlorophenyl-3-methyl-5-phenylpyrazole.

*3-Methyl*-1 : 5-*diphenyl*-4-*pyrazolyl* 3-*Methyl*-1 : 5-*diphenylpyrazole*-4-*thiolsulphonate.*—(*a*) Di-(3-methyl-1 : 5-diphenyl-4-pyrazolyl) disulphide (8 g.) in aqueous acetic acid (containing 20% water by vol.) was treated with a rapid current of chlorine at 0° for 0·5 hr. After a further 0·5 hr. with occasional shaking, the solution was clear. The white solid (5 g., 59%) obtained by addition of ice-water, melted, after several recrystallisations from acetic acid, at 212° (Found: N, 9·65; S, 11·2. $C_{32}H_{26}O_2N_4S_2$ requires N, 9·9; S, 11·4%).

(*b*) The disulphide (2·65 g., 0·005 mol.) in acetic acid (20 c.c.) containing 30% hydrogen peroxide (1 c.c.) was warmed at 100° for 0·5 hr., then left at room temperature with occasional shaking, for 5 days. The white solid (2 g., 70%) was filtered off and, after recrystallisation from acetic acid, melted at 211—212° alone or mixed with the product from method (*a*).

*Reduction of the Thiolsulphonate* (III).—The thiolsulphonate (3 g.) in hot glacial acetic acid (30 c.c.) containing zinc dust (20 g.) was treated with concentrated hydrochloric acid (50 c.c.), in small amounts during 1 hr. After neutralisation with ammonia (*d* 0·880), the precipitated solid was dissolved in hot glacial acetic acid (50 c.c.), and oxidation to the disulphide completed by addition of anhydrous ferric chloride (1 g.) and further heating for 5 min. at 100°. The crystalline precipitate (2·1 g.) from the cooled solution (2·1 g.) melted at 202—204° alone or mixed with di-(3-methyl-1 : 5-diphenyl-4-pyrazolyl) disulphide.

NORTHERN POLYTECHNIC, HOLLOWAY, LONDON, N.7. [*Received, October 28th*, 1957.]

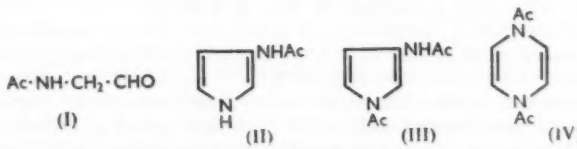
[12] Hunsberger, Shaw, Fugger, Ketcham, and Lednicer, *J. Org. Chem.*, 1956, **21**, 394.

## 231. *Self-condensation of Acetamidoacetaldehyde and of Aminoacetone.*

By J. W. Cornforth.

Acetamidoacetaldehyde in hot, slightly alkaline, aqueous solution gives 3-acetamido-1-acetylpyrrole which is then hydrolysed to 3-acetamidopyrrole. The liquid base $C_6H_{10}N_2$ obtained by Gabriel and Colman from aminoacetone is shown to be a dihydro-2 : 5-dimethylpyrazine.

*N*-Acetylhexosamines, on being heated with mild aqueous alkali, give solutions which become purple on addition of Ehrlich's reagent;[1] the principal biochemical method for analysis of *N*-acetylhexosamines[2] depends on this property. In 1936 Professor W. T. J. Morgan, F.R.S., found that a solution of acetamidoacetaldehyde (I), prepared ***in situ*** by acid hydrolysis of the acetal, behaved similarly and was therefore interesting as a simple model. A crystalline product, m. p. 175—176° (corr.), was isolated from the heated alkaline solution, but its structure was not determined at the time. In 1950, Professor Morgan kindly made a personal communication of his results and the reaction was examined further. Sodium acetate was found to be a suitable base for generating chromogen from the aldehyde (I), and this afforded a crystalline product, m. p. 91—92°, intensely chromogenic to Ehrlich's reagent. Its properties (including a sensitivity to oxidation which defeated attempts to recrystallize it from solvents) and its composition, $C_6H_8ON_2$, pointed to 3-acetamidopyrrole (II) as a probable structure. A Curtius degradation of the known methyl pyrrole-3-carboxylate,[3] the azide being decomposed by boiling acetic acid, gave an identical substance and proved that structure (II) was correct.



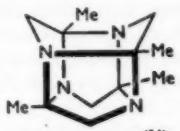

A Knorr synthesis from aminoacetaldehyde and acetamidoacetaldehyde could give the pyrrole (II), but it seemed unlikely that significant hydrolysis of the acetyl group in the aldehyde would occur under such mild conditions. 1-Acetylpyrroles, on the other hand, seem to be hydrolysed readily by alkalis,[4] so that a more likely precursor of the pyrrole (II) was 3-acetamido-1-acetylpyrrole (III). When acetamidoacetaldehyde was heated with aqueous sodium acetate and the solution was extracted every few minutes with ethyl acetate, a crystalline product, m. p. 171°, of the expected composition was isolated, to which the formula (III) is ascribed. It is probably identical with the product obtained in the early experiment. In keeping with its formulation as a 1-acylpyrrole it was relatively stable to air; it gave no colour with Ehrlich's reagent alone, but an intense purple colour was produced when the reagent was added after the substance had been warmed briefly with dilute sodium carbonate solution. The infrared spectrum was of the expected type; in particular, the presence of a band in the N–H stretching region excluded the slight possibility that the substance was an *NN*-diacetyldihydropyrazine (IV).

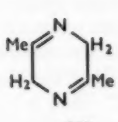
By these observations the production of a chromogen from acetamidoacetaldehyde (I) is explained; but the value of the latter as a model of the more complex *N*-acetylhexosamines has been nullified by Kuhn's work[5] indicating that furans, not pyrroles, are the chromogens in the Morgan–Elson analysis.

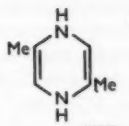
[1] Zuckerkandl and Messiner-Klebermass, *Biochem. Z.*, 1931, **236**, 19.
[2] Morgan and Elson, *Biochem. J.*, 1934, **28**, 988.
[3] Rinkes, *Rec. Trav. chim.*, 1938, **57**, 423.
[4] Ciamician and Dennstedt, *Ber.*, 1883, **16**, 2354.
[5] Kuhn, "Festschrift Prof. Dr. Arthur Stoll," Birkhauser, Basel, 1957, p. 845; and earlier papers there cited.

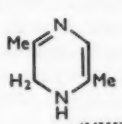
At one stage of this investigation we were interested to know whether simple dihydropyrazines would give coloured solutions with Ehrlich's reagent. Gabriel and Colman [6] described a base $C_6H_{10}N_2$ obtained from aminoacetone hydrochloride and potassium hydroxide. Two forms were obtained, an unstable liquid boiling near 100°/50 mm. and a more stable crystalline solid, m. p. 115—116°, isolated *via* the oxalate. Both forms, the liquid at 139° and the solid at 182°, had vapour densities corresponding to $C_6H_{10}N_2$. Because the liquid base was so unstable, the solid base and its salts were chiefly studied. It gave aminoacetone on acid hydrolysis; but since it could not be directly oxidized to dimethylpyrazine or reduced to dimethylpiperazine Gabriel and Colman were doubtful whether to describe it as a dihydropyrazine and they enumerated five other possible structures.

From the evidence, it seemed likely that the solid base was a polymer, dissociated to monomer when heated, of dihydrodimethylpyrazine. An interesting possibility for a reversible dimerization peculiar to dihydropyrazines is shown in structure (V). The liquid base would then be the monomer, as its boiling point suggests.


(V)


(VI)


(VII)


(VIII)

The present investigation was limited to an examination of the liquid base. The report of its instability was fully confirmed. When it was hydrogenated immediately after preparation, *trans*-2 : 5-dimethylpiperazine was formed and was characterized as its dibenzoyl derivative, thus substantiating the presence of dihydro-2 : 5-dimethylpyrazine in the liquid $C_6H_{10}N_2$. Three structures for the dihydropyrazine are possible: (VI), (VII), and (VIII). The infrared spectrum of the base showed a band at 3260 cm.$^{-1}$ (associated N–H) and a doublet in the double-bond region at 1665 and 1656 cm.$^{-1}$. If the base is substantially homogeneous, the unsymmetrical structure (VIII) is indicated; but a similar spectrum might be given by a mixture of (VI) and (VII). Dihydropyrazines from aminoketones are usually formulated as analogues of (VI) or (VII); yet the conjugated structure (VIII) seems more attractive. The liquid base gave no colour with Ehrlich's reagent.

## Experimental

3-*Acetamidopyrrole* (II).—(i) Acetic anhydride (1·5 ml.) was added to aminoacetaldehyde diethyl acetal (2 g.) and pyridine (2 ml.) in dry ether (20 ml.). After 10 min. potassium carbonate (2·8 g.; freshly ignited) was added; the mixture was shaken occasionally for 2 hr., left overnight, and filtered. Distillation gave acetamidoacetal (2·4 g.), b. p. 72°/0·04 mm., m. p. 20°. This product (1·8 g.) was hydrolysed when heated for 5 min. with 0·1N-hydrochloric acid (50 ml.). The cooled solution was neutralized and saturated with sodium acetate trihydrate, then boiled gently (no reflux) for 2 hr., cooled, and extracted five times with half its volume of ethyl acetate. The evaporated extract was taken up in a little water, and aqueous mercuric chloride was added until precipitation was complete. The collected solid was suspended in water (10 ml.) and decomposed by hydrogen sulphide. The filtered, neutralized solution was extracted thrice with ether. After evaporation the crystalline residue (60 mg.) was purified by two sublimations at 75—90°/0·01 mm. 3-*Acetamidopyrrole* (35 mg.) was a colourless crystalline powder, m. p. 91—92° (Found: C, 58·2; H, 6·3; N, 22·6. $C_6H_8ON_2$ requires C, 58·1; H, 6·5; N, 22·6%). The substance blackened after a few hours in air but a sample has been kept in nitrogen for six years without visible deterioration. A test with Ehrlich's reagent gave an intense purple colour.

(ii) Methyl pyrrole-3-carboxylate (500 mg.) was heated on a steam-bath with 90% hydrazine

[6] Gabriel and Colman, *Ber.*, 1902, **35**, 3805.

hydrate (0·23 ml.) and water (0·3 ml.) for 7 hr. The crystalline hydrazide (484 mg.), m. p. about 120°, obtained by evaporation *in vacuo* was dissolved in N-hydrochloric acid (4 ml.), cooled in ice, and treated with sodium nitrite (276 mg.) in water during 10 min. The dark mixture was extracted with ether; from the dried extract by treatment with charcoal, evaporation, and recrystallization from cold acetone by addition of water, 3-azidocarbonylpyrrole (317 mg.) was obtained as slightly discoloured irregular prisms, decomposing with decrepitation at 105°. Analysis was difficult (Found: N, 43·4. Calc. for $C_5H_4ON_4$: N, 41·2%). The azide (300 mg.) in acetic acid (3 ml.; purified) was boiled until gas evolution appeared complete (8 min.). The cooled solution was evaporated at low pressure and the product, after extraction by ethyl acetate from a considerable blue residue, was purified *via* the mercury complex as described above. Two sublimations gave colourless crystals (42 mg.) (Found: C, 58·1; H, 6·7%), m. p. 91—93° alone or mixed with the specimen obtained as in (i).

3-*Acetamido*-1-*acetylpyrrole* (III).—Acetamidoacetaldehyde diethyl acetal (2 g.) was hydrolysed for a few min. with hot 0·05N-hydrochloric acid (20 ml.). The solution was made faintly alkaline, saturated with sodium acetate, and heated in boiling water. After a few min. the mixture was cooled and extracted twice with ethyl acetate; heating was then continued and the sequence was repeated some ten times. The extracts, on evaporation, left a partly crystalline residue which was sublimed, with rejection of the first sublimate (100°/0·05 mm.) and collection at 110—170°. The product on recrystallization from methanol–ether gave 3-*acetamido*-1-*acetylpyrrole* (50—60 mg.) as colourless leaflets, m. p. 171° (Found: C, 57·6; H, 6·3; N, 17·1. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·0; N, 16·9%); ν (in KCl) 3300 (N–H), 1695 (1-acetyl C=O), 1660 and 1570 cm.$^{-1}$ (NH·CO).

*Experiments with the Liquid Base* $C_6H_{10}N_2$.—The freshly prepared, twice-distilled base [6] (384 mg.) was hydrogenated in ethanol over platinum (from 50 mg. of oxide) at room temperature and pressure. Hydrogen corresponding to 1·6 mols. was taken up overnight. The filtered solution was acidified with hydrochloric acid and evaporated; on treatment with ethanol an insoluble hydrochloride remained. A portion, on being heated with a pellet of potassium hydroxide, gave an iridescent cloud of sublimed four-sided plates, m. p. 117° (*trans*-2 : 5-dimethylpiperazine,[7] m. p. 117°). Another portion gave 1 : 4-dibenzoyl-*trans*-2 : 5-dimethylpiperazine, m. p. 225° (lit.,[7] 224—225°) (Found: C, 74·5; H, 7·0; N, 8·6. Calc. for $C_{20}H_{22}O_2N_2$: C, 74·5; H, 6·8; N, 8·7%).

In another experiment the base was redistilled (b. p. 35°/0·4 mm.) as a colourless mobile liquid which crystallized and melted at about 10°. An infrared spectrum (liquid film) was taken immediately (see above for description). The ultraviolet absorption spectrum (in ethanol) showed maxima at 310 mμ (log ε 2·44) and 275 mμ (log ε 2·97) but since oxygen was not excluded the spectrum may not be that of the original base. The base very rapidly became yellow and viscous on exposure to air. No solvent could be found for a low-temperature crystallization.

I am much indebted to Professor W. T. J. Morgan, F.R.S., for directing attention to this problem.

National Institute for Medical Research,
Mill Hill, London, N.W.7.

[*Received, October 29th*, 1957.]

[7] Bamberger and Einhorn, *Ber.*, 1897, **30**, 227.

## 232. *A Hydrate of Potassium Dichloroiodide.*

By G. F. Allison and G. H. Cheesman.

Potassium dichloroiodide exists as a monohydrate as well as the anhydrous compound.

The compounds $KIBr_2$ and $KICl_2$ were reported by Wells, Wheeler, and Penfield [1] but the analyses given show deficiencies of about 6%. Cremer and Duncan [2] and Cheeseman and Martin,[3] working separately but in association, showed that for the dibromoiodide the analytical deficiency was attributable to the formation of a hydrate $KIBr_2.H_2O$ when the substance was crystallised from or produced in the presence of water. This hydrate gave a dissociation pressure in agreement with values reported by Ephraim,[4] but the anhydrous material gave pressures considerably lower.

Cremer and Duncan [2] maintained that a similar explanation could not be applicable in the case of $KICl_2$, since material dried for several months over phosphoric oxide gave dissociation pressures similar to those reported by Ephraim for material crystallised from water. On the other hand, Cremer and Duncan reported that in the equilibrium $KICl_2$(solid)–KCl(solid)–ICl (in carbon tetrachloride) a concentration of ICl amounting to 0·029N was set up at 25°. This, combined with Blair and Yost's data,[5] corresponds with a dissociation pressure of about 0·6 mm. The pressures reported by Cremer and Duncan (actually measured by Duncan and Cheesman) were 7 mm. at 21·9° and 17 mm. at 31·9°; extrapolation of Ephraim's curve leads to a similar estimate, and these values are more than 10 times larger than those calculated from the experiments in carbon tetrachloride. As it therefore seems possible that the dissociation pressures reported by Cremer and Duncan may be erroneous, and that their conclusion regarding the non-existence of a hydrate of $KICl_2$ was invalid, the question has been re-examined.

Potassium dichloroiodide was prepared by both wet and dry methods and the deficiency in the analysis of the former confirmed and shown to correspond with the formula $KICl_2.H_2O$. Its dissociation pressure accorded well with Ephraim's values and those reported by Cremer and Duncan on reputedly dry material. On the other hand, material prepared by the dry method and enclosed in an apparatus provided with a phosphoric oxide bulb gave much lower dissociation pressures which accord more closely with those estimated from the equilibrium in carbon tetrachloride. Finally, the two materials gave quite distinct *X*-ray diffraction patterns. both of which differ from that of potassium chloride, which might be present in each as an impurity.

The formation of a hydrate also explains the anomalous effect, reported by Cremer and Duncan, of dehydration at the " melting point " of the dichloroiodide.

It thus appears that the dichloroiodide, like $KIBr_2$ and $KI_3$, forms a monohydrate. Of the three, $KI_3$ alone is unknown in the anhydrous state.

### Experimental

The wet method of Wells *et al.*[1] was found most suitable. Sufficient water was added to powdered potassium chloride to produce a thin slurry when boiling (2—3 ml. for 5 g.), and the theoretical amount of finely ground iodine mixed in (8·5 g.). Chlorine was then added, the mixture being kept well stirred and at 80—90°, until all the iodine had dissolved, slightly less than the theoretical amount of chlorine being taken up. Orange crystals up to 15 mm. long formed on cooling (m. p. 50—60° in a sealed tube).

The anhydrous material was prepared by Cremer and Duncan's method. Dry chlorine was

[1] Wells, Wheeler, and Penfield, *Z. anorg. Chem.*, 1892, **1**, 442.
[2] Cremer and Duncan, *J.*, 1931, 2243.
[3] Cheesman and Martin, *J.*, 1932, 2640.
[4] Ephraim, *Ber.*, 1917, **50**, 1069.
[5] Blair and Yost, *J. Amer. Chem. Soc.*, 1933, **55**, 4489.

passed over finely ground potassium dibromoiodide (prepared in the dry way from potassium iodide and bromine) spread on a watch glass in an 8 oz. bottle containing a layer of calcium chloride. The liberated bromine was sucked off and the material reground and spread at intervals until nearly uniform in colour, then stored in the stoppered bottle for ½ hr., after which it was uniformly bright yellow. It was stored in a weighing bottle over phosphoric oxide. It did not melt in a sealed tube but whitened above 200°.

*Analysis.*—The oxidising equivalent of the material was found by adding excess of aqueous potassium iodide and titrating with thiosulphate. Absence of iodate was checked by adding sulphuric acid at the end of the titration. The proportion of volatile constituents was estimated by the conversion into monohalide on gentle ignition.

The following analytical figures were obtained: data for the dibromoiodide are included as it was the starting material for the dichloroiodide:

| | Titre (ml. of N-$Na_2S_2O_3$/g.) | | Loss on ignition (%) | |
|---|---|---|---|---|
| | Found | Calc. | Found | Calc. |
| $KIBr_2$ | 6·13 | 6·14 | 63·66 | 63·48 |
| $KICl_2$ | 8·05, 8·10 | 8·44 | 68·32 | 68·53 |
| $KICl_2,H_2O$ | 7·70, 7·76 | 7·83 | 71·73, 71·68 | 70·74 |

The discrepancies may be due to slight contamination of the dichloroiodide with potassium chloride due to loss of halogen, and the difficulty of drying $KICl_2,H_2O$ completely without risk of excessive decomposition.

*Dissociation Pressures.*—These were measured in a glass-spring manometer similar to that used by Cremer and Duncan. The apparatus was evacuated with a mercury diffusion pump and the sample cooled with liquid oxygen whilst being sealed. With the anhydrous material phosphoric oxide was sublimed into the centre section from an additional side arm, which was then removed before being sealed off from the pumps. This apparatus was set aside for 24 hr. to allow the phosphoric oxide to absorb any small traces of water.

The following pressures were recorded for anhydrous $KICl_2$:

| Temp. (°c) | 32·5 | 53·2 | 71·5 | 81·5 | 92·0 | 100 | 111 | 124 | 132 | 138 |
|---|---|---|---|---|---|---|---|---|---|---|
| Pressure (mm.) | 3·4 | 5·6 | 19·2 | 32·8 | 48·7 | 67·6 | 79·1 | 123·9 | 189·0 | 250·3 |

The agreement of the present observations on the hydrate with those of Ephraim and of Cremer and Duncan, and their relationship with the measurements on the anhydrous material, were demonstrated graphically.

The hydrated material recombined immediately on cooling, whereas the anhydrous was slow, recombination not being complete some 6 days later.

X-*Ray Diffraction Patterns.*—These were obtained with a rotated sealed glass capillary in a 19 cm. camera with unfiltered copper radiation. The hydrous material was packed at low temperature in a deep-freeze unit to minimise decomposition.

The following lines were observed: $KICl_2$: θ = 11·16(w), 12·43(vs), 13·34(w), 13·58(w), 14·46(w), 14·78(vs), 15·96(vw), 16·40(vw), 17·15(w), 19·01(vs), 19·39(w), 21·93(w), 22·84(w), 24·42(s), 25·26(w), 25·98(w), 28·07(w), 28·67(s), 30·03(w), 33·14(s), 38·98(w). $KICl_2,H_2O$: θ = 9·21(w), 9·39(s), 9·87(w), 10·56(w), 10·86(w), 11·01(s), 11·31(s), 12·39(vs), 13·26(w), 13·52(vw) 14·04(s), 14·54(vw), 14·72(vs), 16·34(s), 17·00(vs), 17·60(w), 18·95(vs), 19·33(w), 19·54(s), 19·75(vw), 19·87(vw), 21·18(s), 21·63(w), 21·93(w), 22·12(s), 22·75(w), 23·22(s), 23·74(w), 24·39(s), 24·78(s), 25·23(w), 25·74(w), 25·97(w), 27·17(s), 28·82(s), 29·50(w), 29·92(w), 30·16(w), 31·30(s), 33·34(s), 33·75(w), 34·80(w), 35·40(w), 35·99(w), 36·74(vw), 38·98(vw), 39·89(vw), 40·50(vw), 40·94(vw), 44·22(vw), 46·77(vw), 66·40(vw), 66·68(vw).

UNIVERSITY OF TASMANIA, HOBART.

[*Received, October 29th*, 1957.]

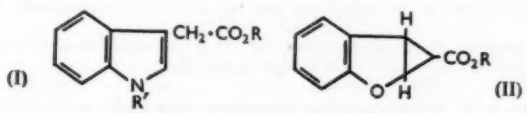
## 233. *Polynuclear Heterocyclic Systems. Part XIII.* The Reaction of Ethyl Diazoacetate with Naphthalene and its Heterocyclic Analogues.*

By G. M. Badger, B. J. Christie, H. J. Rodda, and Jenneth M. Pryke.

Thionaphthen and benzofuran with ethyl diazoacetate yield ethyl 2 : 3-dihydrothionaphthen-2 : 3-yleneacetate (III; R = Et) and 2 : 3-dihydrobenzofur-2 : 3-yleneacetate (II; R = Et) respectively. The structure of the former has been established by reductive desulphurisation to 2-*cyclo*hexyl-*cyclo*propanecarboxylic acid (IV). Under the same conditions, indole and 1-methylindole react with ethyl diazoacetate, by substitution, to give ethyl 3-indolylacetate and 1-methyl-3-indolylacetate (I; R = Et, R′ = H and Me respectively).

Reaction of ethyl diazoacetate with naphthalene yields ethyl 1 : 2 : 3 : 4-tetrahydronaphth-1 : 2-3 : 4-di(yleneacetate) (X; R = Et) as well as the monoadduct (IX; R = Et).

At elevated temperatures ethyl diazoacetate adds to carbon–carbon double bonds, with elimination of nitrogen, to form *cyclo*propane derivatives. The reaction is not confined to ethylenic compounds, and several aromatic hydrocarbons undergo this addition.[1] With polycyclic aromatic hydrocarbons, the addition occurs at the bond having the greatest bond order.[2,3] and ethyl diazoacetate has been classified as a "double-bond reagent."[4] Few attempts have so far been made to apply the reaction to heterocyclic systems, although reaction with thiophen is said to give a *cyclo*propane adduct.[5] On the other hand, pyrrole undergoes substitution to give (after hydrolysis) 2-pyrrylacetic acid.[6] The reaction of ethyl diazoacetate with naphthalene and its heterocyclic analogues has now been investigated.




Indole, 1-methylindole, thionaphthen, and benzofuran were heated with ethyl diazoacetate and the resulting esters distilled and hydrolysed. The acidic product from indole was identified as 3-indolylacetic acid (I; R = R′ = H), and no addition product was obtained. This is a surprising result, but it confirms the findings by previous workers [7,8] who obtained the same acid after hydrolysis of the product obtained by heating indole and ethyl diazoacetate in the presence of copper powder. It is clear that the presence of the copper does not affect the course of the reaction. The acidic hydrogen of indole is also without effect, for 1-methylindole gave 1-methyl-3-indolylacetic acid (I; R = H, R′ = Me), under the same conditions. Its structure was confirmed by direct comparison with a specimen prepared by *N*-methylation of 3-indolylacetic acid.

The acid obtained on reaction of benzofuran with ethyl diazoacetate was not identical with 2- or 3-benzofurylacetic acid. Addition to the 2 : 3-bond was therefore indicated, and the properties of the acid agree with its formulation as 2 : 3-dihydrobenzofur-2 : 3-yleneacetic acid (II; R = H). Its ultraviolet absorption spectrum is given in Fig. 1.

* Part XII, *J.*, 1958, 913.

[1] Badger, "Structures and Reactions of the Aromatic Compounds," Cambridge, 1954.
[2] Buchner and Hediger, *Ber.*, 1903, **36**, 3502.
[3] Badger, Cook, and Gibb, *J.*, 1951, 3456.
[4] Badger, *J.*, 1949, 456.
[5] Steinkopf and Augestad-Jensen, *Annalen*, 1922, **428**, 154.
[6] Piccinini, *Gazzetta*, 1899, **29**, 363.
[7] Jackson and Manske, *Canad. J. Chem.*, 1935, **13**, *B*, 170.
[8] Nametkin, Mel'nikov, and Bokarev, *Zhur. priklad. Khim.*, 1956, **29**, 459; *Chem. Abs.*, 1956, **50**, 13867.

The acid obtained from thionaphthen and ethyl diazoacetate likewise differed from the known 2- and 3-thionaphthenylacetic acid, and a *cyclo*propane addition structure (III) again appeared likely. This was supported by its stability to oxidation, for treatment with permanganate gave only 2 : 3-dihydrothionaphthen-2 : 3-yleneacetic acid 1 : 1-dioxide (VI). The ultraviolet absorption spectrum of the adduct (III; R = H) resembled that of the parent compound rather closely (Fig. 2).

The structure of the adduct (III; R = H) was proved by reductive desulphurisation with W-7 Raney nickel which not only removed the sulphur but simultaneously hydrogenated

FIG. 1. FIG. 2.

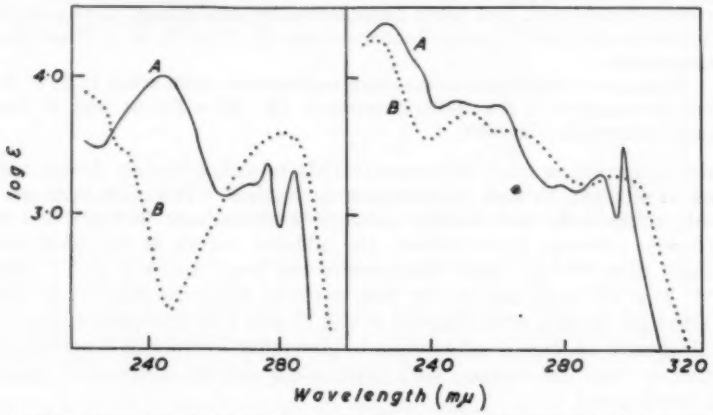
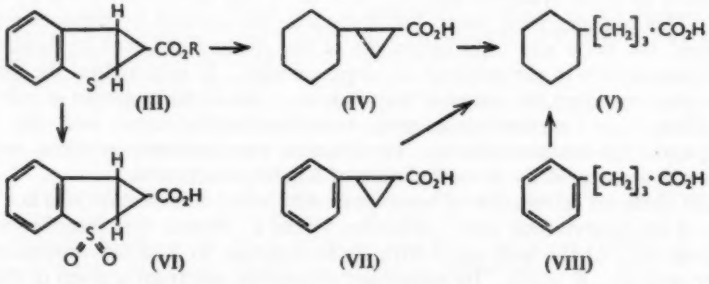



FIG. 1. *Ultraviolet absorption of (A) benzofuran and (B) 2 : 3-dihydrobenzofur-2 : 3-yleneacetic acid* (II) *in* 95% EtOH.

FIG. 2. *Ultraviolet absorption of (A) thionaphthen and (B) 2 : 3-dihydrothionaphthen-2 : 3-yleneacetic acid* (III) *in* 95% EtOH.

the benzene ring to give 2-*cyclo*hexyl*cyclo*propanecarboxylic acid (IV) (characterised as the amide). This result was surprising; for 2-phenyl*cyclo*propanecarboxylic acid (VII) was expected; but all attempts to bring about the desulphurisation with less active




catalysts were either unsuccessful or gave the same hydrogenated product. Moreover, both *cis*- and *trans*-2-phenyl*cyclo*propanecarboxylic acid (VII) were recovered unchanged after treatment with W-7 Raney nickel under " desulphurisation " conditions. It seems that the hydrogenation must proceed by addition of hydrogen to some other intermediate (possibly of a radical nature) formed after removal of the sulphur. In this reaction the *cyclo*propane ring must be important, for no hydrogenation of the benzene ring is observed in the desulphurisation of 3-thionaphthenylacetic acid.[9]

[9] Blicke and Sheets, *J. Amer. Chem. Soc.*, 1948, **70**, 3768.

With Adams catalyst, both *cis*- and *trans*-2-phenyl*cyclo*propanecarboxylic acid were hydrogenated to γ-*cyclo*hexylbutyric acid (V); this was also obtained by similar hydrogenation of 2-*cyclo*hexyl*cyclo*propanecarboxylic acid (IV) or γ-phenylbutyric acid (VIII). These examples of the reductive fission of *cyclo*propanes under relatively mild conditions, with Adams catalyst, parallel that recorded by Linstead and his co-workers,[10] who obtained ethyl *n*-butylmalonate from ethyl 2-vinyl*cyclo*propane-1 : 1-dicarboxylate. In all these cases rupture of the *cyclo*propane ring occurs at the bond linking the two substituents.

Buchner and Hediger [2] have shown that ethyl diazoacetate also reacts with naphthalene by addition. Hydrolysis of the adduct gave 1 : 2-dihydro-1 : 2-naphthyleneacetic acid (IX; R = H), the structure of which was firmly established. Conjugation of the *cyclo*propane ring with the 3 : 4-bond [1] would be expected to reduce the ethylenic nature of

FIG. 3. FIG. 4.

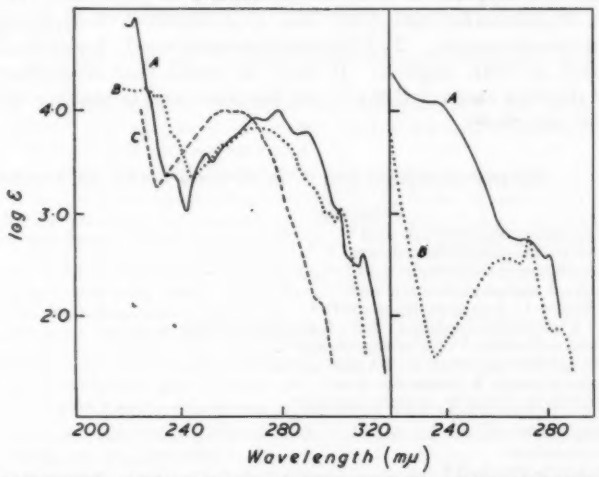
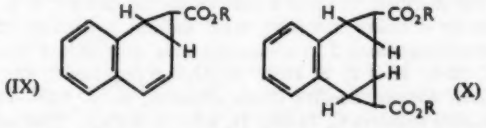



FIG. 3. *Ultraviolet absorption of* (*A*) *ethyl* 1-*naphthylacetate and* (*B*) *ethyl* 1 : 2-*dihydro*-1 : 2-*naphthyleneacetate, in* 95% EtOH, *and of* (*C*) 1 : 2-*dihydronaphthalene in* $C_6H_6$ (Hückel, Vevera, and Wörffel, *Chem. Ber.*, 1957, **90**, 901).

FIG. 4. *Ultraviolet absorption of* (*A*) *ethyl* 1 : 2-3 : 4-*tetrahydronaphth*-1 : 2-3 : 4-*di*(*yleneacetate*) *and* (*B*) *tetralin, in* 95% EtOH.

this bond; and its reactivity would also be affected by the electron-attracting effect of the ethoxycarbonyl group, and by steric hindrance. Nevertheless, the formation of a monoadduct as the sole product is unexpected, and the reaction of naphthalene with ethyl




diazoacetate has accordingly been re-investigated. On careful fractionation, the monoadduct (IX; R = Et) was obtained as the major product; but a little diadduct (X; R = Et) was also isolated. The same product was obtained when the monoadduct was heated with a further quantity of ethyl diazoacetate. Hydrolysis of this diadduct gave 1 : 2-3 : 4-tetrahydronaphth-1 : 2-3 : 4-di(yleneacetic acid) (X; R = H). This was not identical with 1 : 4- or 1 : 5-naphthylenediacetic acid, and its structure is supported by the ultraviolet absorption spectrum of the diester (X; R = Et) (Fig. 4).

[10] Kierstead, Linstead, and Weedon, *J.*, 1952, 3610.

Several authors [11] have pointed out that *cyclo*propane derivatives all show a moderately strong absorption infrared band between 1000 and 1050 cm.$^{-1}$. *cyclo*Propane itself [12] has a peak at 1028·7 cm.$^{-1}$, which has been assigned to a ring-bending vibration, and many substituted *cyclo*propanes absorb around 1021 ± 5 cm.$^{-1}$. All of our *cyclo*propanes examined had an absorption peak in this region (see Table) but its diagnostic value with heterocyclic derivatives must be accepted with great caution. 3-Indolylacetic acid (I; R = R′ = H), 1-methyl-3-indolylacetic acid (I; R = H, R′ = Me), and 3-thionaphthenylacetic acid all gave a similar peak in this region, although not containing a *cyclo*propane ring. Moreover, other simple indoles absorb in this region.[13]

3-Indolylacetic acid (I; R = H) is a potent plant hormone (auxin). So Dr. N. P. Kefford of the C.S.I.R.O., Canberra, very kindly tested our materials, using the *Avena* section test. 3-Indolylacetic, 1-methyl-3-indolylacetic, and 3-thionaphthenylacetic acid [14] all showed auxin activity; but 2 : 3-dihydrobenzofur-2 : 3-yleneacetic (II), 2 : 3-dihydrothionaphthen-2 : 3-yleneacetic acid (III), and 1 : 2-dihydro-1 : 2-naphthyleneacetic acid were active as auxin *antagonists*. 2 : 3-Dihydrothionaphthen-2 : 3-yleneacetic acid dioxide (VI) was inactive in both respects. It may be noted that *cis*-2-phenyl*cyclo*propanecarboxylic acid displays auxin activity,[15] but the *trans*-acid is inactive both as an auxin and as an auxin antagonist.

*Infrared absorption* (cm.$^{-1}$) *in the* 1000—1050 *cm.*$^{-1}$ *region.*[a]

| Compound | Frequency |
|---|---|
| *cis*-2-Phenyl*cyclo*propanecarboxylic acid [b] | 1025 w |
| *trans*-2-Phenyl*cyclo*propanecarboxylic acid [b] | 1026 w |
| 2-*cyclo*Hexyl*cyclo*propanecarboxylic acid [c] | 1031 m |
| 1 : 2-Dihydro-1 : 2-naphthyleneacetic acid [b] | 1012 w |
| Ethyl 1 : 2-dihydro-1 : 2-naphthyleneacetate [d] | 1025 m |
| Ethyl 1 : 2-3 : 4-tetrahydronaphth-1 : 2-3 : 4-di(yleneacetate) | 1026 s |
| 2 : 3-Dihydrothionaphthen-2 : 3-yleneacetic acid [b] | 1018 m |
| Ethyl 2 : 3-dihydrothionaphthen-2 : 3-ylene acetate [d] | 1031 m |
| 2 : 3-Dihydrobenzofur-2 : 3-yleneacetic acid [b] | 1015 w |
| Ethyl 2 : 3-dihydrobenzofur-2 : 3-ylene acetate [c] | 1036 m |
| 3-Indolylacetic acid [b] | 1010 w |
| Ethyl 3-indolylacetate [c] | 1026 s |
| 1-Methyl-3-indolylacetic acid [b] | 1012 m |
| 3-Thionaphthenylacetic acid [b] | 1019 w |

[a] NaCl prism. [b] Nujol mull. [c] Liquid film. [d] In $CHCl_3$.

## Experimental

2 : 3-*Dihydrothionaphthen*-2 : 3-*yleneacetic Acid.*—Ethyl diazoacetate (25 g.) was added with stirring during 7 hr. to thionaphthen (65 g.) at 145—150°. Evolution of nitrogen began after 15 min. and continued throughout the addition. After a further hour's stirring and heating, the product was distilled, to yield a pale yellow oil (5·5 g.), b. p. 113—120°/0·04 mm., which was hydrolysed by 4 hours' refluxing with sodium hydroxide (2 g.) in 95% ethanol (30 c.c.). 2 : 3-*Dihydrothionaphthen*-2 : 3-*yleneacetic acid* crystallised from hexane in needles, m. p. 150° (Found: C, 62·6; H, 4·2; S, 16·6. $C_{10}H_8O_2S$ requires C, 62·5; H, 4·2; S, 16·7%). Its 4-*phenylphenacyl ester* formed needles (from ethanol), m. p. 129—130° (Found: C, 74·3; H, 4·6; S, 8·1. $C_{24}H_{18}O_3S$ requires C, 74·55; H, 4·7; S, 8·3%). The *amide*, prepared *via* the acid chloride, separated from water in needles, m. p. 225° (Found: S, 16·5. $C_{10}H_9ONS$ requires S, 16·8%).

The acid (1 g.) in dilute sodium carbonate was treated with potassium permanganate. After 18 hr. at room temperature, and 4 hr. on the steam-bath the excess of permanganate was

[11] Slabey, *J. Amer. Chem. Soc.*, 1954, **76**, 3604; Mohrbacher and Cromwell, *ibid.*, 1957, **79**, 401.
[12] Baker and Lord, *J. Chem. Phys.*, 1955, **23**, 1636.
[13] Brown, Henbest, and Jones, *J.*, 1952, 3172.
[14] See also Kefford and Kelso, *Austral. J. Biol. Sci.*, 1957, **10**, 80.
[15] Veldstra and Van de Westeringh, *Rec. Trav. chim.*, 1951, **70**, 1127.

removed and the solution acidified. **2 : 3-*Dihydrothionaphthen*-2 : 3-*yleneacetic acid* 1 : 1-*dioxide*** separated from water in needles, m. p. 240—241° (Found: C, 53·5; H, 3·8; S, 14·3. $C_{10}H_8O_4S$ requires C, 53·6; H, 3·6; S, 14·3%). It showed infrared (Nujol mull, NaCl prism) bands at 1136 and 1312 cm.$^{-1}$ characteristic of sulphones.

A solution of the acid (2 g.) in 10% aqueous sodium carbonate (20 c.c.) was added to a stirred suspension of W-7 Raney nickel (15 g.) in water (250 c.c.). The mixture was heated for 1 hr. on the steam-bath, filtered, and acidified. The oily product was extracted with ether, and the ether dried ($CaSO_4$), and evaporated, to yield 2-*cyclo*hexyl*cyclo*propanecarboxylic acid. Its amide, prepared *via* the acid chloride, crystallised from water in needles, m. p. 151° unchanged by further purification; but a completely satisfactory analysis could not be obtained (Found: C, 71·3; H, 10·9; N, 8·3. Calc. for $C_{10}H_{17}ON$: C, 71·8; H, 10·3; N, 8·4%).

*γ*-cyclo*Hexylbutyric Acid*.—(i) *trans*-2-Phenyl*cyclo*propanecarboxylic acid was hydrogenated in ethanol at 60° over Adams catalyst, at atmospheric pressure. The resulting oil was converted *via* its acid chloride into *γ-cyclo*hexylbutyramide, which crystallised from water in needles, m. p. 109—110° alone or admixed with a specimen prepared by similar hydrogenation of *γ*-phenylbutyric acid.

(ii) Similar hydrogenation of *cis*-2-phenyl*cyclo*propanecarboxylic acid likewise gave *γ-cyclo*hexylbutyramide.

(iii) Catalytic hydrogenation of 2-*cyclo*hexyl*cyclo*propanecarboxylic acid in 50% ethanol over Adams catalyst was also effected at 60°, and yielded *γ-cyclo*hexylbutyramide. The infrared spectra of these amides were identical.

**2 : 3-*Dihydrobenzofur*-2 : 3-*yleneacetic Acid*.**—Ethyl diazoacetate (23 g.) was added with stirring during 3 hr. to benzofuran (50 g.) at 150°. After being stirred at this temperature for a further 4 hr. the mixture was distilled, to give a yellow oil (7·5 g.), b. p. 93—100°/0·04 mm. Hydrolysis with alcoholic sodium hydroxide gave **2 : 3-*dihydrobenzofur*-2 : 3-*yleneacetic acid***, which crystallised from dilute ethanol in plates, m. p. 181—181·5° (Found: C, 68·1; H, 4·65; O, 26·9. $C_{10}H_9O_3$ requires C, 68·2; H, 4·6; O, 27·2%). The ***amide*** formed needles (from water), m. p. 198—199° (Found: C, 68·2; H, 5·2. $C_{10}H_9O_2N$ requires C, 68·5; H, 5·2%).

**3-*Indolylacetic Acid*.**—Ethyl diazoacetate (25 g.) was added with stirring during 4 hr. to indole (60 g.) at 140° (no catalyst was added; cf. refs. 7 and 8) and the temperature maintained for a further hr. Distillation gave indole (26 g.; b. p. 134°/18 mm.), and a crude product (23 g., b. p. 142—144°/0·1 mm.) which was hydrolysed with alcoholic sodium hydroxide. The resulting 3-indolylacetic acid recrystallised from water and from benzene–light petroleum and had m. p. and mixed m. p. 164—165°.

**1-*Methyl*-3-*indolylacetic Acid*.**—(i) Ethyl diazoacetate (13·1 g.) was treated with 1-methylindole (15 g.) as above.[6] After a fore-run of 1-methylindole (3 g.; b. p. 46°/0·05 mm.) the crude product (12·3 g., b. p. 116°/0·05 mm.) was obtained. The acid obtained by hydrolysis recrystallised from water and from benzene–light petroleum as needles, m. p. 128° alone or mixed with a specimen prepared as described below. The picrate formed red needles, m. p. 171° (decomp.) (lit., m. p. 174°, 161°).

(ii) 3-Indolylacetic acid (1 g.) was added to a solution of sodium (0·29 g.) in liquid ammonia (20 c.c.). Methyl sulphate (2 c.c.) was added dropwise to the stirred solution during 15 min., and stirring continued for 1 hr.[16] After evaporation of the ammonia, methanol and then water were added. Removal of the methanol and acidification gave the crude acid, which recrystallised from benzene–light petroleum, to give 1-methyl-3-indolylacetic acid as needles, m. p. 128° (lit., m. p. 127—129°).

*Reaction of Ethyl Diazoacetate with Naphthalene*.—(i) Ethyl diazoacetate (23 g.) was added dropwise during 6 hr. to naphthalene (50 g.) at 140° (bath-temperature) (cf. ref. 2). The mixture was distilled, and after a fore-run of naphthalene the fraction of b. p. 112—180°/0·15 mm. was collected. Re-distillation gave the crude monoadduct, b. p. 94—120°/0·05 mm. (7·5 g.), and a residue (6 g.) which was chromatographed in light petroleum on alumina. Trituration of the resulting yellow oil with light petroleum gave a solid product which was re-chromatographed and repeatedly recrystallised from light petroleum. ***Ethyl* 1 : 2-3 : 4-*tetrahydronaphth*-1 : 2-3 : 4-*di*(*yleneacetate*)** was obtained as prisms, m. p. 89° (Found: C, 72·2; H, 6·7; O, 21·1. $C_{16}H_{20}O_4$ requires C, 72·0; H, 6·7; O, 21·3%). When tested with osmium tetroxide in pyridine the monoadduct showed the presence of a reactive double bond, but the diacetate remained unchanged. Hydrolysis of this diester was effected with alcoholic potassium

[16] Cf. Plieninger, *Chem. Ber.*, 1954, **87**, 127.

XUM

hydroxide. Recrystallisation from aqueous ethanol gave **1 : 2-3 : 4-*tetrahydronaphth*-1 : 2-3 : 4-*di*(*yleneacetic acid*)** (X) as needles, m. p. 286° (Found: C, 68·9; H, 5·1; O, 26·0. $C_{14}H_{12}O_4$ requires C, 68·8; H, 4·95; O, 26·2%).

(ii) The same diester was obtained on addition of ethyl diazoacetate (8 g.) to the mono-adduct (9 g.) at 145° during ½ hr. and further heating for 1½ hr.

Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne. One of us (B. J. C.) has been working with an I.C.I.A.N.Z. Fellowship. We also thank Dr. N. P. Kefford for the biological tests.

UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA. [*Received, October 29th*, 1957.]

---

## 234. *The Stereochemistry of Triarylstibines. Part II.* Synthesis of Unsymmetrically Substituted Triarylstibines and Optical Resolution of* p-*Carboxyphenyl*-1-*naphthylphenylstibine.*

By I. G. M. CAMPBELL and A. W. WHITE.

The synthesis of five stibines of the type $p$-$HO_2C{\cdot}C_6H_4{\cdot}SbPhAr$ is described. Models of these compounds indicate that two are sterically hindered, and one of these (Ar = 1-naphthyl) has been separated into (+)- and (−)-forms, $[\alpha]_D^{18}$ ±35·5° ± 1·5° (in $CHCl_3$), which are optically stable. No hindrance to the free rotation of the groups around the antimony atom is indicated in the other three, consequently they should be suitable compounds for testing the stability of the pyramidal configuration of tervalent antimony by attempted optical resolution.

IN Part I* the difficulties met in the synthesis of the unsymmetrical diarylstibinous chlorides ArAr'SbCl necessary for the preparation of triarylstibines suitable for stereochemical investigation were outlined. At that time the only known stibinous chlorides of this type contained a 2-diphenylyl group and attempts to obtain others by the route illustrated had failed at the initial step.

$$Ar{\cdot}N_2SbCl_4 + p\text{-}EtO_2C{\cdot}C_6H_4{\cdot}SbCl_2 \xrightarrow[-Cu]{EtOH} p\text{-}EtO_2C{\cdot}C_6H_4{\cdot}SbCl_2{\cdot}Ar + N_2 + SbCl_3$$
(I)

$$(I) \xrightarrow[-EtOH]{SnCl_2} p\text{-}EtO_2C{\cdot}C_6H_4{\cdot}SbClAr \xrightarrow{PhMgBr} p\text{-}EtO_2C{\cdot}C_6H_4{\cdot}SbArPh\ (III)$$
(II)

$$\xrightarrow{Hydrol.} p\text{-}HO_2C{\cdot}C_6H_4{\cdot}SbArPh\ (IV)$$

The striking difference between the ease of isolating the trichloride (I) when Ar was the 2-diphenylyl group and the complete failure when Ar was $p$-bromophenyl, $p$-chlorophenyl, or 4-diphenylyl seemed to indicate that an *ortho*-substituent in the diazonium salt was essential for success. This prompted the use of the diazonium double salts from $o$-chloroaniline and $o$-toluidine, but in neither case was the required compound obtained. Attempts were then made with 3-aminodiphenyl, *p-cyclo*hexylaniline, and 1- and 2-naphthylamine, as these bases would provide trichlorides having approximately the same molecular weight as the 2-diphenylyl derivatives and possibly also similar melting points. It was then found that the earlier lack of success in obtaining compounds of type (I) can be ascribed, not to the failure of the reaction, but to the difficulty of isolating the product.

In the 2-diphenylyl series the trichlorides crystallise readily, whereas compounds containing other aryl groups remain dissolved in the ethanolic mixture and there undergo decomposition or disproportionation. The latter occurred in attempts to prepare (I;

* Part I, *J.*, 1955, 3116.

Ar = *o*-Me·$C_6H_4$ or *o*-Cl·$C_6H_4$), the product, in each case, being di-*p*-ethoxycarbonylphenylstibinic chloride. Similarly, in the initial experiment with *p-cyclo*hexylaniline, disproportionation occurred, but in this case the di-*p-cyclo*hexylphenyl derivative was isolated. Either of the two symmetrical compounds can evidently separate from the reaction mixture, but, so far, it has proved impossible to isolate both. This type of redistribution is not uncommon among compounds of this type and has been observed in similar syntheses of unsymmetrical arsinic [1] and phosphinic acids.[2]

The unsymmetrical trichlorides were isolated in several cases by extraction with benzene and dilute hydrochloric acid. But the compounds which separated from benzene tenaciously retained variable amounts of the solvent; this led to variable melting points and analyses and made it much more difficult to characterise the pure compounds.

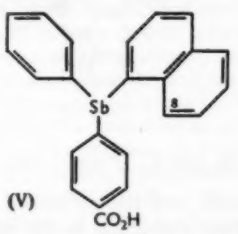
Reduction of the tri- to the mono-chlorides (the second step in the route) also gave trouble until it was realised that the concentration of hydrochloric acid in the ethanol–stannous chloride medium was critical, and that even moderate concentrations encouraged fission of the carbon–antimony bond, thus:

$$p\text{-EtO}_2\text{C}\cdot\text{C}_6\text{H}_4\cdot\text{SbClAr} + \text{HCl} \longrightarrow p\text{-EtO}_2\text{C}\cdot\text{C}_6\text{H}_4\text{SbCl}_2 + \text{ArH}$$

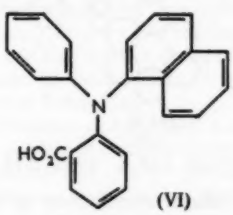
For example, the monochloride (II; Ar = 1-naphthyl), which crystallised well from the ethanol–stannous chloride reaction mixture, when washed with 2N-hydrochloric acid to remove tin salts and then dried *in vacuo* at room temperature, decomposed rapidly into naphthalene and *p*-ethoxycarbonylphenylstibonous chloride.

A further difficulty, which remains unsolved, is the apparent ease with which the chloride (II; Ar = 3-diphenylyl), obtained as a viscous oil, is re-oxidised in air to a quinquevalent antimony derivative.

Conversion of the diarylstibinous chlorides (II), into the triarylstibines (III) by interaction with phenylmagnesium bromide gave the stibine esters as viscous gums from which no crystalline dichlorides or dibromides could be obtained, although bromine was absorbed in approximately the calculated quantity. This is again in contrast to experience in the 2-diphenylyl series (see Part I) where the preparation of pure dibromides permitted the initial isolation of the crystalline stibine esters. However, hydrolysis of the crude products from the Grignard reaction gave the acids (IV), though they were obtained pure only after



(V)



(VI)

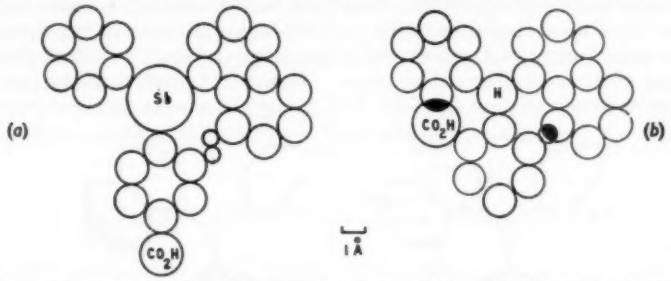
very wasteful crystallisations. The low yield obtained in this reaction was further reduced in the case of the 2-naphthyl isomer because, apparently at some stage in the isolation, oxidation occurred and a portion of the product proved to be the insoluble, high-melting oxide of the triarylstibinecarboxylic acid.

*p*-Carboxyphenyl-1-naphthylphenylstibine (IV; Ar = 1-naphthyl) was readily resolved into (+)- and (−)-forms by crystallisation of the (−)- and (+)-1-phenylethylamine salts, the (+)-base forming the least soluble salt with the (−)-acid. The more soluble (+)-base-(+)-acid salt was not obtained optically pure. The acids, $[\alpha]_D^{18}$ ±35·5° ± 1·5°, were stable in chloroform and in ethanol at room temperature and in boiling *p*-xylene for two hours. Prolonged boiling in the last solvent produced an opalescent solution

[1] Campbell and Poller, *J.*, 1956, 1200; Poller, Ph.D. Thesis, Southampton, 1955, p. 38.
[2] Doak and Freedman, *J. Amer. Chem. Soc.*, 1952, **74**, 2884.

which made further polarimetric measurements impossible, but the enantiomers obviously possess considerable optical stability. Loss of activity was observed on one occasion only, when a solution in chloroform was left for more than a week in intermittent sunlight. Analysis indicated that some decomposition had occurred: the (±)-acid is light-sensitive and develops a buff to brown colour on prolonged exposure.

A model of this stibine (V), in which the atoms are represented by spheres with normal covalent radii and the antimony atom has a planar arrangement of bonds, indicates that on rotation of the groups, the hydrogen atom at position 8 of the naphthyl group just touches the hydrogens on the *ortho*-positions of the two benzene rings. A Courtauld model,[3] in which the atoms have van der Waals radii and the bonds from antimony are set at the tetrahedral angle, indicates interference, although the restriction to the rotation of the groups is not great—it is, in fact, considerably less than in models of a similar nitrogen compound, *N*-1-naphthyl-*N*-phenylanthranilic acid (VI) whether the bonds from nitrogen are planar, tetrahedral, or pyramidal. In this molecule, the small diameter of nitrogen and the presence of the *ortho*-carboxy-group results in such restriction that the 1-naphthyl group is virtually locked in a plane at right angles to the two phenyl groups. Scale diagrams (Figure, *a* and *b*), in which the nitrogen and antimony bond angles are taken as 120° and restriction is consequently at a minimum, indicate that in the nitrogen compound (VI) the *o*-carboxyphenyl group overlaps both the phenyl group and the 1-naphthyl group, whereas no such overlap occurs in the antimony analogue (V). As covalent radii have been used in the Figures, the restriction is undoubtedly underestimated, but the difference in degree of overcrowding in the two molecules is clear, and, judged on this basis, since stable (+)- and (−)-forms of the antimony compound (V) have been obtained, isolation of enantiomers of the analogue (VI) would be expected. Nevertheless, Meisenheimer and his collaborators were unable to obtain any evidence of resolution, although they examined both the strychnine and the brucine salts of this acid (VI).




C–C, 1·4 Å. C–$CO_2H$, 1·56 Å. C–Sb, 2·11 Å. C–N, 1·44 Å. ∠CSbC, 120°. ∠CNC, 120°.

The failure to isolate enantiomers of the amine and the successful resolution of the stibine lend support to the suggestion (Part I) that restriction in the nitrogen compound is rendered ineffective by the rapid inversion of the pyramidal configuration, whereas the barrier to inversion in the stibine is sufficiently high to permit the isolation of stable optical antipodes. Further, the results again confirm Weston's prediction, derived from calculations,[5] that optical isomers of tervalent nitrogen compounds should racemise even at very low temperatures, whereas those of antimony should be stable above room temperature.

## Experimental

p-cyclo*Hexylaniline*.—Phenyl*cyclo*hexane was nitrated by a modification of Turner and Mayes's method.[6] Nitric acid (145 ml.; *d* 1·5) in glacial acetic acid (60 ml.) was added in 0·5

[3] Hartley and Robinson, *Trans. Faraday Soc.*, 1952, **48**, 847.
[4] Meisenheimer, Angermann, Finn, and Vieweg, *Ber.*, 1924, **57**, 1744.
[5] Weston, *J. Amer. Chem. Soc.*, 1954, **76**, 2645.
[6] Turner and Mayes, *J.*, 1929, 500.

hr. to phenyl*cyclo*hexane (36 ml.) in acetic acid (72 ml.) at 18—20°. The mixture was stirred for a further 0·5 hr., poured on ice, and extracted with benzene. The oil obtained from benzene extraction in three such experiments was distilled through a heated Vigreux column and separated into fractions, b. p. 138—142°/0·3 mm. and 145—150°/0·3 mm. The second fraction solidified and crystallised from ethanol to give *p-cyclo*hexylnitrobenzene, m. p. 58° (64 g.). Refractionation of the lower-boiling oil gave a first cut, b. p. 96°/6 × $10^{-3}$ mm., which solidified at −10° and crystallised from ethanol to give the *ortho*-isomer, m. p. 45° (Neunhoeffer [7] gives m. p. 45°). From the residue a further 10 g. of the *para*-compound was isolated.

Reduction of this with iron filings and boiling water at 100° gave *p-cyclo*hexylaniline, m. p. 50—55°, in almost quantitative yield, but catalytic reduction gave a purer product. In this method, the nitro-compound (34·2 g.) was reduced in ethanol (200 ml.) at 60° with hydrogen (5 atm.) and Adams platinum catalyst (0·2 g.). The filtered solution was evaporated, leaving the pure amine, m. p. 54—55° (27·2 g., 93%).

*3-Aminodiphenyl.*—3-Nitrodiphenyl was prepared by the Gomberg procedure of Elks, Haworth, and Hey [8] from *m*-nitrobenzenediazonium chloride, benzene, and aqueous sodium acetate. The crude product, b. p. 150°/0·85 mm., crystallised from ethanol and had m. p. 58—60° (47%). This was reduced catalytically under conditions identical with those used in the previous experiment to an amine, m. p. 28—30·5° (acetyl derivative, m. p. 149·5—150°; Fichter and Sulzberger [9] report m. p. 148°).

*3-Amino-4-methoxydiphenyl.*—The method recommended by Tarbell, Hirschler, and Hall [10] was used for this preparation. Coupling 4-hydroxydiphenyl with benzenediazonium chloride gave the 3-azo-compound, m. p. 128—130°, which was converted into the methyl ether, m. p. 139°. Reduction of the azo-compound with stannous chloride proved unsatisfactory because an intractable stannichloride was obtained; the use of sodium dithionite gave *4-methoxy-3-phenylhydrazodiphenyl*, m. p. 141° (Found: C, 78·7; H, 6·4. $C_{19}H_{18}ON_2$ requires C, 78·6; H, 6·2%). Catalytic reduction at 60° gave the required amine, m. p. 83°, in almost quantitative yield (ref. 10 gives m. p. 80—81°).

*Preparation of the Stibinic Chlorides* (I).—The arylamine (0·1 mole) was diazotised in concentrated hydrochloric acid (25 ml.) and water (50 ml.) by solid sodium nitrite (7 g.) at 0—5°. The filtered diazonium salt solution was added to antimony trioxide (16 g.) dissolved in concentrated hydrochloric acid (100 ml.) at −10° to 0°, and the precipitated double salt was filtered off and washed with ice cold ethanol. This was added to a solution of *p*-ethoxycarbonylphenylstibonous chloride (30 g., 0·088 mole) in ethanol (100 ml.). Decomposition of the double salt occurred between 30° and 50°, depending on the nature of the aryl group, and, when evolution of nitrogen ceased, the dark mixture was shaken in a separatory funnel with benzene (100 ml.) and 4N-hydrochloric acid (150 ml.). This usually resulted in the separation of three zones, benzene, acid, and a heavy oil; the last was further extracted with benzene and acid, and the combined extracts dried and evaporated to small bulk. From this concentrated solution the trichloride separated in the cases listed in Table 1(*a*).

Alternatively, when this procedure gave the trichloride in low yield, a solution of pyridine (10 ml.) in concentrated hydrochloric acid (25 ml.) was added to the ethanolic reaction mixture, and the precipitated pyridinium tetrachloroantimonate was filtered off and crystallised from ethanol containing hydrochloric acid. The properties of the salts are recorded in Table 1(*b*). The 3-diphenylyl derivative could not be crystallised satisfactorily except from ethyl acetate and it retained this solvent. Stirring with 2% sodium carbonate for 12 hr. decomposed the tetrachloroantimonate to give the stibinic acid from which the corresponding trichloride was obtained by trituration of the moist acid with cold concentrated hydrochloric acid.

When *o*-toluidine, *o*-chloroaniline, or *p*-bromoaniline was used in this reaction, the required unsymmetrical compound was not obtained. Instead, di-*p*-ethoxycarbonylphenylstibinic chloride, m. p. 183—184° (decomp.), was isolated although not analytically pure (Found: C, 40·0; H, 3·9. Calc. for $C_{18}H_{18}O_4Cl_2Sb$: C, 41·1; H, 3·4%). Alternatively, addition of pyridine hydrochloride in concentrated hydrochloric acid precipitated *pyridinium di-p-ethoxycarbonylphenyl tetrachloroantimonate*, m. p. 244° (decomp.) (Found: C, 42·9; H, 3·6. $C_{23}H_{24}O_4NCl_4Sb$ requires C, 43·0; H, 3·8%). The trichloride was readily reduced by stannous

[7] Neunhoeffer, *J. prakt. Chem.*, 1932, **133**, 95.
[8] Elks, Haworth, and Hey, *J.*, 1940, 1284.
[9] Fichter and Sulzberger, *Ber.*, 1904, **37**, 882.
[10] Tarbell, Hirschler, and Hall, *J. Amer. Chem. Soc.*, 1953, **75**, 1958.

XUM

chloride in ethanol (see below) to the *monochloride*, m. p. 134·5—135° (Found: C, 47·3; H, 3·8; Sb, 26·6%. $C_{16}H_{13}O_4ClSb$ requires C, 47·5; H, 4·0; Sb, 26·7%).

*Unsymmetrical Diarylstibinous Chlorides* (II).—The trichloride was dissolved in the minimum volume of ethanol, and twice the calculated quantity of stannous chloride was added at room temperature. In favourable cases the monochloride crystallised rapidly on cooling of the reaction mixture, and was filtered off and washed with 0·5N-hydrochloric acid. If the monochloride failed to separate, dilute hydrochloric acid was added until a faint turbidity appeared and cooling gave a crystalline deposit. Frequently, attempted recrystallisation of these

TABLE 1. (*a*) *Stibinic chlorides* (I). *p*-$EtO_2C{\cdot}C_6H_4{\cdot}SbCl_3{\cdot}Ar$.

| | | Yield | | Found (%) | | Required (%) | |
|---|---|---|---|---|---|---|---|
| Ar | M. p. | (%) | Formula | C | H | C | H |
| * *p*-Me·$C_6H_4$ ..... | 129° | 39 | $C_{16}H_{16}O_2Cl_4Sb$ | 44·6 | 4·1 | 41·0 | 3·4 |
| | | | $C_{16}H_{16}O_2Cl_3Sb,\frac{1}{2}C_6H_6$ | | | 45·0 | 3·8 |
| *p-cyclo*-$C_6H_{11}{\cdot}C_6H_4$ ... | 133—134 | 36 | $C_{21}H_{24}O_2Cl_3Sb$ | 46·2 | 4·5 | 47·0 | 4·5 |
| 1-Naphthyl ..... | 135—136 | 18 | $C_{19}H_{16}O_2Cl_3Sb$ | 44·9 | 3·4 | 45·2 | 3·2 |
| 2-Naphthyl ..... | 189—190 | 33 | $C_{19}H_{16}O_2Cl_3Sb$ | 44·7 | 3·3 | 45·2 | 3·2 |
| 3-Diphenylyl ..... | 140 | 20 | $C_{21}H_{18}O_2Cl_3Sb$ | 47·3 | 3·7 | 47·5 | 3·4 |
| 4-OMe-3-diphenylyl... | 162—165 | 15 | $C_{22}H_{20}O_3Cl_3Sb$ | 47·0 | 3·9 | 47·1 | 3·6 |

(*b*) *Diaryl pyridinium tetrachloroantimonates*, $[p\text{-}EtO_2C{\cdot}C_6H_4{\cdot}SbArCl_4]^-[C_5H_6N]^+$.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *p*-Me·$C_6H_4$ ..... | 230° | — | $C_{21}H_{22}O_2NCl_4Sb$ | 43·2 | 3·9 | 43·2 | 3·8 |
| † *p-cyclo*-$C_6H_{11}{\cdot}C_6H_4$ | 240° (decomp.) | 36 | $C_{26}H_{30}O_2NCl_4Sb$ | 48·4 | 4·5 | 47·9 | 4·6 |
| 1-Naphthyl ..... | 216—218 | 30 | $C_{24}H_{22}O_2NCl_4Sb$ | 46·3 | 3·5 | 46·5 | 3·6 |
| 3-Diphenylyl ..... | 117—122 (decomp.) | — | $C_{26}H_{24}O_2NCl_4Sb,C_4H_8O_2$ | 49·3 | 4·2 | 49·1 | 4·4 |

* After 8 hr. at 100°/15 mm., m. p. 115—120° (Found: C, 41·1; H, 3·8%).
† Found: Sb, 18·8. Required: Sb, 18·7%.

precipitated monochlorides gave sticky oils. That this was caused by partial decomposition of the monochloride by hydrochloric acid, was proved when *p*-ethoxycarbonylphenyl-1-naphthylstibinous chloride, which readily separated without addition of acid, was washed with 2N-hydrochloric acid and dried *in vacuo*. After 12 hr. the material, originally highly crystalline, had become pasty, and naphthalene, m. p. 75—80°, had sublimed. The residue, after being washed with ether, had m. p. 124—127° alone or mixed with *p*-ethoxycarbonylphenylstibinous chloride. The properties of the monochlorides are recorded in Table 2.

TABLE 2. *Stibinous chlorides* (II), *p*-$EtO_2C{\cdot}C_6H_4{\cdot}SbCl{\cdot}Ar$.

| | | | Found (%) | | Required (%) | |
|---|---|---|---|---|---|---|
| Ar | M. p. | Formula | C | H | C | H |
| *p*-Me·$C_6H_4$ ..... | 63—66° | $C_{16}H_{15}O_2ClSb$ | 48·0 | 4·2 | 48·3 | 4·1 |
| *p-cyclo*-$C_6H_{11}{\cdot}C_6H_4$ ..... | 110—111 | $C_{21}H_{24}O_2ClSb$ | 54·1 | 4·5 | 54·2 | 5·2 |
| 1-Naphthyl ..... | 90 | $C_{19}H_{16}O_2ClSb$ | 52·8 | 4·0 | 52·6 | 3·7 |
| 2-Naphthyl ..... | 93·5—95 | $C_{19}H_{16}O_2ClSb$ | 52·3 | 4·1 | 52·6 | 3·7 |
| 4-OMe-3-diphenylyl ..... | 154—155 | $C_{22}H_{20}O_2ClSb$ | 54·2 | 4·0 | 54·0 | 4·1 |

In the reduction of (I; Ar = 3-diphenylyl) by this method, an oil was precipitated on addition of acid and this was extracted with ether. Evaporation of the ether left a glass which was soluble in benzene. After 12 hr. in a desiccator this glass was only partly miscible with benzene, and the solid residue remaining, after crystallisation from *cyclo*hexane, had m. p. 144·5—145·5° and proved to be the *hydroxy-dichloride* (Found: C, 49·9; H, 3·5. $C_{21}H_{19}O_3Cl_2Sb$ requires C, 49·3; H, 3·7%). This was treated with 4N-hydrochloric acid and then crystallised from benzene, to give the trichloride, m. p. 130—131° (Found: C, 47·3; H, 3·7%). Similar results were obtained when titanous chloride was used, although decolorisation of the reagent indicated complete reduction. The trichloride was also regained when reduction by sulphur dioxide [11] was attempted.

*Triarylstibines* (IV).—Phenylmagnesium bromide prepared from bromobenzene (3·14 g.,0·02

[11] Lesslie and Turner, *J.*, 1934, 1170.

mole) and magnesium (0·5 g.) in ether (20 ml.) was added during 10 min. to a cooled solution of the monochloride (0·01 mole) in benzene (30 ml.). The addition produced a thick cream-coloured precipitate which gradually became crystalline as the mixture was boiled for 0·25 hr. It was then cooled in ice and shaken with saturated ammonium chloride. The organic layer frequently emulsified at this stage and occasionally it was necessary to filter it from traces of finely divided solid before separation was possible. Removal of the solvents left a pale yellow viscous syrup in all cases. Attempts to crystallise the stibine esters failed and addition of chlorine or bromine in carbon tetrachloride gave no crystalline compound, except in one case (III; Ar = 4-methoxy-3-diphenylyl). In this case chlorine was passed into a solution of the syrup (2·4 g.) in carbon tetrachloride (15 ml.) at <0°. Addition of light petroleum (b. p. 60—80°) precipitated a gum from which the supernatant liquid was decanted. Crystals formed in this liquid and these initiated crystallisation in the gum when triturated with ethanol. The crude product (2·1 g.) was recrystallised from ethanol–ethyl acetate and gave *p-ethoxycarbonylphenyl-4-methoxy-3-diphenylylphenylstibine dichloride*, m. p. 168—169° (Found: C, 55·5; H, 4·3. $C_{28}H_{25}O_3Cl_2Sb$ requires C, 55·9; H, 4·2%).

In the other four cases the syrup (4 g.) obtained from the Grignard reaction was hydrolysed by boiling it for 0·5 hr. with 4% ethanolic potassium hydroxide (100 ml.). The mixture was poured into water (400 ml.) and extracted with ether. From the clear aqueous solution, dilute hydrochloric acid precipitated the triarylstibinecarboxylic acids as fine powders. After drying *in vacuo* for 24 hr., crystallisation gave the pure acids (IV) with properties listed in Table 3.

TABLE 3. *Triarylstibinecarboxylic acids* (IV), *p*-$HO_2C{\cdot}C_6H_4{\cdot}$SbPhAr.

| | | | Yield | | Found (%) | | | Required (%) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Ar | M. p. | Solvent | (%) | Formula | C | H | Sb | C | H | Sb |
| *p*-$MeC_6H_4$ ..... | 161—163° | EtOH | 10 | $C_{20}H_{17}O_2Sb$ | 58·7 | 4·8 | 29·6 | 58·4 | 4·2 | 29·6 |
| *p-cyclo*-$C_6H_{11}{\cdot}C_6H_4$ | 165—166 | $AcOH{\cdot}H_2O$ | 25 | $C_{25}H_{25}O_2Sb$ | 62·8 | 4·9 | 25·2 | 62·7 | 5·3 | 25·4 |
| 1-Naphthyl ..... | 195—196 | $EtOH{\cdot}CHCl_3$ | 38 | $C_{23}H_{17}O_2Sb$ | 62·0 | 3·7 | 26·9 | 61·8 | 3·8 | 27·2 |
| 2-Naphthyl ..... | 170 | $EtOH{\cdot}CHCl_3$ | 18 | $C_{23}H_{17}O_2Sb$ | 62·2 | 4·0 | 27·0 | 61·8 | 3·8 | 27·2 |
| 4-OMe-3-di-phenylyl ..... | 196—197 | EtOH | 20 | $C_{26}H_{21}O_3Sb$ | 62·2 | 4·0 | — | 62·1 | 4·2 | 24·2 |

When the crude acid (IV; Ar = 2-naphthyl) was crystallised, the first fraction to separate had m. p. >270° and proved to be the *oxide* (Found: C, 59·7; H, 4·0. $C_{27}H_{17}O_3Sb$ requires C, 59·6; H, 3·7%). The second fraction was the acid, m. p. 170°.

*Optical Resolution of* p-*Carboxyphenyl-1-naphthylphenylstibine.*—(Rotations of salts were measured in " AnalaR " chloroform at room temp.; $l = 2$; $c$, 0·25—0·35).

In a preliminary experiment, the acid (0·45 g.) was suspended in hot ethanol (5 ml.), and (+)-1-phenylethylamine (0·25 g.) added. Complete dissolution occurred but no salt separated overnight. Addition of ether precipitated a gel which, in 3 hr. became crystalline and was filtered off. This salt (0·27 g.) had m. p. 162—176°, $[\alpha]_D$ −5·0°, raised by one crystallisation from ethyl acetate to $[\alpha]_D$ −14·8°. A second small fraction of salt (0·06 g.) separated slowly from the original preparation and had m. p. 158—180°, $[\alpha]_D$ +45·5°, but the residues formed a glass from which no further crystals could be isolated.

As this appeared to be definite evidence of resolution, the experiment was repeated on a larger scale. The acid (2·2 g.) was added to (+)-1-phenylethylamine (1·2 g., 2 equivs.) in hot ethanol (12 ml.). Immediate dissolution occurred but almost immediate separation of gelatinous crystals [2·35 g.; over 80% of the total (2·8 g.)]. This material was extracted with boiling ethyl acetate (30 ml.), leaving *salt* F1, $[\alpha]_D$ 0° (1·7 g.), and from the extract there separated 0·4 g. of salt, $[\alpha]_D$ +4·6°. Salt F1 was recrystallised twice from ethanol–chloroform and then had m. p. 185°, $[\alpha]_D$ −21·0° ± 0·9° (0·35 g.), unchanged on further recrystallisation (Found: C, 65·2; H, 5·3%. $C_{23}H_{17}O_2Sb,C_6H_{11}N$ requires C, 65·5; H, 5·0%). Working up intermediate fractions yielded a further 0·31 g. of the pure (−)-acid–(+)-base salt, but no fraction as strongly dextrorotatory as that obtained in the initial trial was isolated. Decomposition of the residual salts gave acid $[\alpha]_D$ +6·7° (in $CHCl_3$).

To obtain the (+)-acid, the resolution was repeated with (−)-1-phenylethylamine. The acid (0·85 g.) and (−)-base (0·5 g.) were dissolved together in 8 ml. of hot ethanol. Overnight hard rosettes of tiny needles separated, and had $[\alpha]_D$ +12·7° (0·32 g.). These were recrystallised from ethanol and then had m. p. 185—186°, $[\alpha]_D$ +20·8° ± 1° (0·11 g.) (Found: C, 65·1; H, 5·4%).

XUM

*Isolation of (+)- and (−)-acids.* The (−)-acid–(+)-base salt (0·21 g.) was dissolved in ethanol (25 ml.) and cooled to −10°. Addition of 0·1N-sulphuric acid gave a milky separation and dilution with water precipitated the (−)-acid, which was filtered off, washed, and dried (0·11 g.). It had an indefinite m. p. (91—100°), $[\alpha]_D^{18}$ −35·5° ± 1·5° (*c* 0·324 in " AnalaR " $CHCl_3$), $[\alpha]_D^{22}$ −30·5° (*c* 0·328 in " AnalaR " benzene) (Found: C, 62·2; H, 4·2. $C_{23}H_{17}O_2Sb$ requires C, 61·8; H, 3·8%).

The (+)-acid–(−)-base salt, decomposed similarly, gave the (+)-acid, m. p. 92—100°, $[\alpha]_D^{18}$ +35·1° ± 1·6° (*c* 0·314 in " AnalaR " $CHCl_3$), $[\alpha]_D^{22}$ +27·1° (*c* 0·259 in 99·6% EtOH) (Found: C, 62·0; H, 4·2%).

*Attempted Racemisation.*—The (−)-acid (0·0433 g.) was dissolved in *p*-xylene (99·6%; b. p. 138°) (20 ml.) and had $\alpha_D^{18}$ −0·13°, $[\alpha]_D^{18}$ −30·0°. The solution was boiled for 0·5 hr. under reflux, then rapidly cooled to 18°; the rotation was unchanged. After a further 1·5 hours' heating there was still no change in rotation. When the solution had been heated for 8 hr. a faint opalescence made further readings impossible. The (+)-acid (0·0620 g.), $\alpha_D^{22}$ +0·19°, showed no change in rotation after 2 hours' boiling, but again a faint precipitate was obtained on further heating.

The authors thank the Chemical Society and Imperial Chemical Industries Limited for financial assistance. A. W. White is indebted to the Department of Scientific and Industrial Research for a maintenance allowance.

THE UNIVERSITY, SOUTHAMPTON. [*Received, October 30th,* 1957.]

---

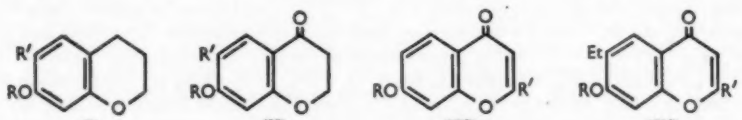
## 235. 7-*Hydroxychroman and its* 6-*Acetyl Compound.*

By P. NAYLOR, G. R. RAMAGE, and F. SCHOFIELD.

Resorcinol and β-chloropropionyl chloride gave 7-hydroxychroman-4-one which was reduced to 7-hydroxychroman. This formed a 6-acetyl compound as was shown by reduction to the 6-ethyl compound, which was also prepared from 4-ethylresorcinol.

6-ACETYL-7-HYDROXYCHROMAN (I; R = H, R′ = Ac) was required for the synthesis of various dihydropyranochromones. Several routes to 7-hydroxychroman were examined, one of which involved many stages and was an extension of the route to 7-hydroxychromone-2-carboxylic acid (III; R = H, R′ = $CO_2H$) reported by Jacobson, Brower, and Amstutz.[1] Recently Gregory and Tomlinson [2] prepared the 7-benzyloxy-compound (II; R = $CH_2Ph$, R′ = H) but failed with the debenzylation stage.

7-Hydroxychroman-4-one (II; R = R′ = H) was conveniently obtained from resorcinol and β-chloropropionyl chloride in nitrobenzene by the action of aluminium chloride. The initial product was extracted with aqueous sodium hydroxide and this brought about the necessary ring closure, forming 7-hydroxychroman-4-one, and not the alternative coumarin or 5-membered ring compound. The chromanone was characterised




by derivatives and reduced, by hydrogen and a Raney nickel catalyst, to 7-hydroxychroman (I; R = H, R′ = H). This gave the 6-acetyl compound (I; R = H, R′ = Ac)

[1] Jacobson, Brower, and Amstutz, *J. Org. Chem.*, 1953, **18**, 1117.
[2] Gregory and Tomlinson, *J.*, 1956, 795.

when treated with acetic anhydride and aluminium chloride under Friedel–Crafts conditions, or by a Fries rearrangement of its *O*-acetyl derivative (I; R = Ac, R′ = H). The position of the acetyl group was established by its reduction to an ethyl group and the identity of the resulting product (I; R = H, R′ = Et) with that derived from 4-ethylresorcinol.

For the alternative synthesis, the slightly modified route of Jacobson *et al.*[1] was used. A Claisen condensation with ethyl oxalate and 4-benzyloxy-5-ethyl-2-hydroxyacetophenone gave ethyl 4-benzyloxy-5-ethyl-2-hydroxybenzoylpyruvate, which was converted into 6-ethyl-7-hydroxychromone (IV; R = H, R′ = H) by cyclisation, hydrolysis, debenzylation, and decarboxylation. The resulting chromone (IV; R = H, R′ = H) was reduced in two stages and gave the chroman-4-one (II; R = H, R′ = Et) and then 6-ethyl-7-hydroxychroman (I; R = H, R′ = Et). This route was also used to prepare 7-hydroxychroman-4-one and in this way the identity of the product from resorcinol and β-chloropropionyl chloride was confirmed.

## Experimental

*4-Benzyloxy-5-ethyl-2-hydroxyacetophenone.*—5-Ethyl-2 : 4-dihydroxyacetophenone [3] (49 g.) and powdered anhydrous potassium carbonate (42 g.) were added to a cold solution of sodium iodide (50 g.) in dry acetone (300 c.c.), followed by benzyl chloride (43 c.c.), and the mixture gently refluxed with stirring for 5 hr. After removal of the acetone, the mixture was digested with warm water (500 c.c.) and the product filtered. Crystallisation from ethanol (charcoal) gave 4-benzyloxy-5-ethyl-2-hydroxyacetophenone (66 g., 90%) as needles, m. p. 106° (Found: C, 76·1; H, 6·8. Calc. for $C_{17}H_{18}O_3$: C, 75·5; H, 6·7%). Jacobson *et al.*[1] gave 50%.

*Ethyl 7-Benzyloxychromone-2-carboxylate* (III; R = $CH_2Ph$, R′ = $CO_2Et$).—Ethyl 4-benzyloxy-2-hydroxybenzoylpyruvate [1] (27 g.) was refluxed for 1 hr. with ethanolic hydrogen chloride (250 c.c.; 12% w/v), cooled, and filtered. On crystallising the residue from ethanol, *ethyl 7-benzyloxychromone-2-carboxylate* (III; R = $CH_2Ph$, R′ = $CO_2Et$) was obtained as needles (24 g., 94%), m. p. 172° (Found: C, 70·3; H, 4·9. Calc. for $C_{19}H_{16}O_5$: C, 70·4; H, 5·0%).

A similar preparation from ethyl 4-benzyloxy-5-ethyl-2-hydroxybenzoylpyruvate [1] gave *ethyl 7-benzyloxy-6-ethylchromone-2-carboxylate* (IV; R = $CH_2Ph$, R′ = $CO_2Et$) (22 g., 86%) as needles (from ethanol), m. p. 111—112° (Found: C, 71·4; H, 5·4. $C_{21}H_{20}O_5$ requires C, 71·6; H, 5·7%).

*7-Hydroxychromone-2-carboxylic Acid* (III; R = H, R′ = $CO_2H$).—Concentrated hydrochloric acid (100 c.c.) was added to a solution of the ester (III; R = $CH_2Ph$, R′ = $CO_2Et$) (10·5 g.) in ethanol (100 c.c.), and the suspension was refluxed for 6 hr. and then cooled. Water (200 c.c.) was added and the mixture filtered. The residue was purified by dissolving it in, and reprecipitating it from, dilute sodium hydroxide solution, followed by washing with water and crystallisation from methanol. *7-Hydroxychromone-2-carboxylic acid* (5 g., 75%) formed needles, m. p. 312° (decomp.) (Found: C, 58·2; H, 3·3. $C_{10}H_6O_5$ requires C, 58·3; H, 2·9%).

*7-Hydroxychromone* (III; R = R′ = H).—The acid (III; R = H, R′ = $CO_2H$) (2 g.) was heated at 300—310° for 5 min. and cooled. The product was extracted with boiling water, and 7-hydroxychromone (0·8 g., 50%) recovered on cooling as colourless needles, m. p. 221° (Found: C, 66·6; H, 3·9. Calc. for $C_9H_6O_3$: C, 66·7; H, 3·7%).

*7-Hydroxychroman-4-one* (II; R = R′ = H).—(*a*) Raney nickel catalyst (10 c.c.; settled suspension in ethanol) was shaken with a solution of 7-hydroxychromone (3 g.) in methanol (150 c.c.) in hydrogen until the hydrogen uptake reached 470 c.c. (*ca.* 3 hr.). The catalyst was filtered off and washed with methanol. Evaporation, at low temperature and pressure, of the combined filtrate and washings left a residue which on crystallisation from water gave 7-hydroxychroman-4-one (2·4 g., 79%) as needles, m. p. 149°.

(*b*) A solution of resorcinol (11 g.) in dry nitrobenzene (120 c.c.) was cooled below 8° and β-chloropropionyl chloride (12·7 g., 9·6 c.c.) added. The solution was stirred and anhydrous resublimed aluminium chloride (31 g.) added in four portions during 30 min., while the temperature of the mixture was kept below 15°. Then the mixture was stirred for 15 min., finally

[3] Shah and Mehta, *J. Univ. Bombay*, 1935, **4**, 109.

XUM

at 40—45° for 3 hr., and next day poured on crushed ice (200 g.) and concentrated hydrochloric acid (10 c.c.) with stirring. The mixture was extracted with ether (220 c.c. and 2 × 80 c.c.), and the combined ethereal extracts were shaken with 5% aqueous sodium hydroxide (3 × 100 c.c.). The combined extracts were washed with ether (80 c.c.), before being added to concentrated hydrochloric acid (80 c.c.) and ice (100 g.), with stirring. The resulting tar was filtered off and crystallised from water (charcoal), and gave 7-hydroxychroman-4-one (7·5 g., 46%) as colourless needles, m. p. 149°, identical with the above material.

7-Hydroxychroman-4-one formed a *semicarbazone*, m. p. 237—238° (decomp.), which crystallised from 50% aqueous ethanol as prisms (Found: C, 54·8; H, 5·0. $C_{10}H_{11}O_3N_3$ requires C, 54·3; H, 5·0%).

*7-Hydroxychroman* (I; R = R′ = H).—Raney nickel catalyst (10 c.c.; settled suspension in ethanol) was shaken with a solution of 7-hydroxychroman-4-one (3 g.) in ethanol (150 c.c.) at 40—45° in hydrogen. When the uptake had ceased (*ca.* 24 hr.) the mixture was cooled and filtered and the catalyst washed with ethanol. Removal of the ethanol under reduced pressure left a brown residue which was distilled (100—120°/0·3 mm.) on to a cold finger. The resulting 7-hydroxychroman (2·13 g., 77%) crystallised from *cyclo*hexane as colourless plates, m. p. 91° (Found: C, 72·2; H, 6·5. Calc. for $C_9H_{10}O_2$: C, 72·0; H, 6·7%).

*7-Acetoxychroman* (I; R = Ac, R′ = H).—A solution of 7-hydroxychroman (4·5 g.) in acetic acid (6 c.c.) and acetyl chloride (2·4 g.) was warmed for 2 min. and then poured into water (35 c.c.). When shaken, the product solidified and was then filtered off and crystallised from aqueous ethanol, to yield *7-acetoxychroman* (4·7 g., 82%), m. p. 50° (Found: C, 69·0; H, 6·2. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%).

*6-Acetyl-7-hydroxychroman* (I; R = H, R′ = Ac).—(*a*) 7-Acetoxychroman (1·0 g.) was ground with resublimed anhydrous aluminium chloride (0·85 g.) and heated slowly to 120°, kept thereat for 15 min., and then cooled. The complex was decomposed with ice (9 g.) and concentrated hydrochloric acid (1 c.c.), and the product filtered off, dried, and crystallised from light petroleum (b. p. 40—60°), to yield *6-acetyl-7-hydroxychroman* (0·62 g., 62%) as prisms, m. p. 93° (Found: C, 68·7; H, 6·5. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%).

(*b*) A similar experiment at room temperature, using 7-acetoxychroman (1·0 g.), resublimed anhydrous aluminium chloride (0·85 g.), and dry nitrobenzene (2 c.c.), yielded 6-acetyl-7-hydroxychroman (0·31 g., 31%) identical with the above material.

(*c*) A solution of 7-hydroxychroman (8·5 g.) in dry nitrobenzene (85 c.c.) and acetic anhydride (6 c.c.) was stirred at 0° and resublimed anhydrous aluminium chloride (16·5 g.) was added in four portions during 30 min., as described for the preparation of 7-hydroxychroman-4-one. The product was filtered off, dried, and extracted with light petroleum (b. p. 40—60°), to yield 6-acetyl-7-hydroxychroman (5·02 g., 46%) as prisms, m. p. 93°.

6-Acetyl-7-hydroxychroman formed a *semicarbazone*, prismatic needles (from ethanol), m. p. 304° (decomp.) (Found: C, 58·5; H, 5·9. $C_{12}H_{15}O_3N_3$ requires C, 57·8; H, 6·1%), and a 2 : 4-*dinitrophenylhydrazone*, orange needles (from dioxan), m. p. 304° (decomp.) (Found: C, 54·0; H, 4·3. $C_{17}H_{16}O_6N_4$ requires C, 54·8; H, 4·3%).

*7-Benzyloxy-6-ethylchromone-2-carboxylic Acid* (IV; R = $CH_2Ph$, R′ = $CO_2H$).—The ester (IV; R = $CH_2Ph$, R′ = $CO_2Et$) (10 g.) was refluxed with 5N-hydrochloric acid (200 c.c.) for 5 hr., and the cooled product, in the form of a hard ball, was removed mechanically. Crystallised from ethanol, *7-benzyloxy-6-ethylchromone-2-carboxylic acid* was obtained as flocculent needles (7·4 g., 80%), m. p. 248° (decomp.) (Found: C, 69·8; H, 4·8. $C_{19}H_{16}O_5$ requires C, 70·4; H, 5·0%). A small amount of 6-ethyl-7-hydroxychromone-2-carboxylic acid (0·7 g., 11%) was isolated from the dilute hydrochloric acid, and crystallised from ethanol as needles, m. p. 293—294° (decomp.) (Found: C, 61·6; H, 4·3. Calc. for $C_{12}H_{10}O_5$: C, 61·5; H, 4·3%).

*7-Benzyloxy-6-ethylchromone* (IV; R = $CH_2Ph$, R′ = H).—A solution of the acid (IV; R = $CH_2Ph$, R′ = $CO_2H$) (5 g.) in pure dry quinoline (25 c.c.) was refluxed with copper bronze powder (2·5 g.) for 20 min., cooled, and acidified with dilute hydrochloric acid. The mixture was extracted with ether (2 × 100 c.c.), and the combined extracts were washed with 5% sodium carbonate solution (100 c.c.) and then water (50 c.c.). Evaporation of the dried ($Na_2SO_4$) ethereal solution left a residue which on crystallisation from *cyclo*hexane gave *7-benzyloxy-6-ethylchromone* (2·5 g., 58%) as pale yellow needles, m. p. 105° (Found: C, 77·3; H, 5·7. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·8%).

*6-Ethyl-7-hydroxychromone* (IV; R = R′ = H):—(*a*) The benzyloxy-compound (IV; R = $CH_2Ph$, R′ = H) (5 g.) was refluxed for 5 hr. with 5N-hydrochloric acid (200 c.c.), filtered

hot, and cooled. The product was removed by filtration and on crystallisation from ethanol gave *6-ethyl-7-hydroxychromone* (2·0 g., 60%) as needles, m. p. 230° (Found: C, 69·3; H, 5·3. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·3%).

(*b*) The acid (IV; R = H, R′ = $CO_2H$) (2·34 g.) was heated for 5 min. at 300°. Distillation of the residue under reduced pressure gave 6-ethyl-7-hydroxychromone (1·04 g., 55%) as a yellow solid which crystallised from ethanol as colourless needles, m. p. 230°, identical with the above material.

*6-Ethyl-7-hydroxychroman-4-one* (II; R = H, R′ = Et).—(*a*) Raney nickel catalyst (5 c.c.; settled suspension in ethanol) was added to a solution of 6-ethyl-7-hydroxychromone (2·5 g.) in ethanol (100 c.c.). The mixture was shaken at 45° in hydrogen until the uptake reached 360 c.c. (*ca.* 3½ hr.); it was then cooled and filtered and the catalyst washed with ethanol. The filtrate and washings were concentrated to about 25 c.c., hot water (25 c.c.) was added, and the solution cooled. *6-Ethyl-7-hydroxychroman-4-one* (2·2 g., 88%) formed plates, m. p. 159° (Found: C, 68·8; H, 6·4. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%).

(*b*) 4-Ethylresorcinol [4] (13·8 g.) was subjected to a Friedel–Crafts reaction as described for the preparation of 7-hydroxychroman-4-one. 6-Ethyl-7-hydroxychroman-4-one (6 g., 31%) crystallised from water (charcoal) as plates, m. p. 159°, identical with the above material.

6-Ethyl-7-hydroxychroman-4-one formed a *semicarbazone*, m. p. 258° (decomp.), which was crystallised from water (Found: C, 57·8; H, 5·9. $C_{12}H_{15}O_3N_3$ requires C, 57·8; H, 6·1%).

*6-Ethyl-7-hydroxychroman* (I; R = H, R′ = Et).—(*a*) A solution of 6-ethyl-7-hydroxychroman-4-one (1·0 g.) in ethanol (100 c.c.) and 10% palladium–charcoal catalyst (0·5 g.) were shaken together at 45° in hydrogen until the uptake ceased (*ca.* 24 hr.). The mixture was filtered and the catalyst washed with ethanol. Evaporation of the filtrate and washings under reduced pressure left a brown oil which was distilled (105—115°/0·9 mm.) on to a cold finger. *6-Ethyl-7-hydroxychroman* crystallised from light petroleum (b. p. <40°) as colourless prismatic needles (0·8 g., 86%), m. p. 69—70° (Found: C, 74·2; H, 8·0. $C_{11}H_{14}O_2$ requires C, 74·1; H, 7·9%).

(*b*) 6-Acetyl-7-hydroxychroman (1·0 g.) and amalgamated zinc (10 g.) were refluxed gently with 4N-hydrochloric acid (30 c.c.) for 4 hr. and cooled. The mixture was extracted with ether (2 × 15 c.c.), and the combined extracts were washed with water (15 c.c.) and dried ($Na_2SO_4$). Evaporation of the ether left a brown oil which on purification as above gave 6-ethyl-7-hydroxychroman (0·75 g., 81%), identical with the above material.

6-Ethyl-7-hydroxychroman formed an *O-carboxymethyl derivative* (I; R = ·$CH_2$·$CO_2H$, R′ = Et), m. p. 161—162°, which crystallised from benzene as needles (Found: C, 66·0; H, 6·5. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%).

The authors thank the Governors of the Royal Technical College, Salford, for the award of a College Demonstratorship (to P. N.).

THE TECHNICAL COLLEGE, HUDDERSFIELD.
THE ROYAL TECHNICAL COLLEGE, SALFORD.

[*Received, November 11th*, 1957.]

[4] Clemmensen, *Ber.*, 1914, **47**, 54.

## 236. *The Steric Course of Alkylation of Enols from Some* cyclo*Hexanones and of Hydrogenation of Selin-4-en-3-ones in Neutral and Alkaline Solution.*

By R. Howe and F. J. McQuillin.

Alkylation of 2 : 5-substituted *cyclo*hexanones is shown to occur preferentially on the face of the molecule where the 5-substituent already is. Hydrogenation of (+)-α- and (+)-*epi*-α-cyperone in alkaline ethanol has been used to characterise a series of *cis*-dihydro- and *cis*-tetrahydro-derivatives and to obtain information about the processes involved; by using alkaline ethanol as solvent, it is possible to hydrogenate preferentially the double bond of the CH:CH·CO group without saturation of the isolated 11 : 12-olefinic double bond.

We have earlier reported [1] the reduction of (+)-*epi*- (I) and natural (+)-α-cyperone (V). Later work disclosed that the two *cis*-tetrahydro-ketones (III) and (VII) described contained some 5 : 10-*trans*-material. By hydrogenating the cyperones in alkaline solution we have now been able to obtain these two *cis*-tetrahydro-ketones in a pure state and also the two *cis*-dihydro-derivatives (IV) and (VIII), thus completing the series of four tetrahydro- and four dihydro-cyperones having the 4-methyl substituent in the stable configuration. The remaining pair of 11 : 12-dihydro-cyperones was described earlier.[1] In the course of this work we have also obtained information on (i) the effect of the side-chain orientation at $C_{(7)}$ on the proportions of *cis*- and *trans*-products formed on hydrogenation, (ii) a parallel influence of the 4-methyl substituent, (iii) the effect of acidity and alkalinity in determining the relative rates of hydrogenation of an enone and an isolated olefinic double bond, and also in influencing the mobility of the olefinic bond at a catalyst surface (cf. Howe and McQuillin [1]), (iv) the stereochemistry of the tetrahydrocyperone synthesised by Bradfield, Jones, and Simonsen.[2] The last point will first be considered.

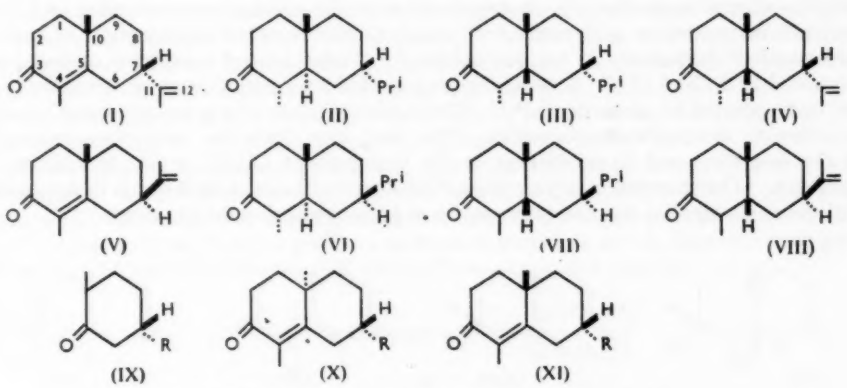
Simonsen and his co-workers, by alkylation of (−)-tetrahydrocarvone (IX*a*) with ethyl β-chloropropionate, followed by a Reformatsky condensation with ethyl α-bromopropionate, obtained a dihydrocyperone which was characterised by hydrogenation to a crystalline tetrahydro-ketone, m. p. 102—103°, $[\alpha]_{5461}$ +22·2°, as the main product. Through the courtesy of the late Sir John Simonsen we have been able to show, by comparison of the semicarbazones, that this substance is the same as the *cis*-tetrahydro-*epi*-α-cyperone (III) (m. p. 98°, $[\alpha]_{5461}$ +23·2°) which we obtained [1] by hydrogenation of the ketone (XI*a*). The discrepant melting point of the ketones has been shown to be due to the presence in both preparations of a little of the corresponding *trans*-tetrahydro-*epi*-α-cyperone (II), which we obtained earlier (m. p. 67°) by reduction of the ketone (XI*a*) with lithium in liquid ammonia. Rigorous crystallisation of our *cis*-tetrahydro-*epi*-α-cyperone has now raised the melting point to 108° ($[\alpha]_{5461}$ +24·0°). This material gives a 2 : 4-dinitrophenylhydrazone, m. p. 123°; the same derivative of the *trans*-ketone, m. p. 67°, has m. p. 222° and from a mixture of the two derivatives the latter, which is much the less soluble, separates readily on crystallisation from ethyl acetate. The 2 : 4-dinitrophenylhydrazone, m. p. 221—223°, reported by Bradfield, Jones, and Simonsen proved to be identical with the latter which was also obtained from the 2 : 4-dinitrophenylhydrazone of lower-melting specimens of our *cis*-tetrahydro-*epi*-α-cyperone.

This identification of the ketones (II) and (III) establishes (XI) as the stereochemical structure of the principal product of Simonsen's synthetic method. By the somewhat different Mannich-base metho-salt condensation, (−)-dihydrocarvone (IX*b*) was previously shown [3] to yield the ketones (X*b*) and (XI*b*) in a ratio of ~1 : 4. By the same method

[1] Howe and McQuillin, *J.*, 1956, 2670.
[2] Bradfield, Jones, and Simonsen, *J.*, 1936, 1137.
[3] McQuillin, *J.*, 1955, 528; Howe and McQuillin, *J.*, 1955, 2423.

XUM

Abe, Harukawa, Ishikawa, Miki, and Toga [4] obtained from the (±)-ester (IX*c*) a product in which the corresponding (11-epimeric) isomers (XI*c*) predominated. Thus in these three alkylations, involving the *cyclo*hexenolate ion derived from the ketones (IX*a*, *b*, and *c*), the alkyl group becomes attached to the face of the molecule already carrying the substituent R, to give on cyclisation mainly the sterically less stable isomer. Other instances may be noted: Johnson, Christiansen, and Ireland,[5] using a monocyclic but heavily substituted *cyclo*hexanone, report a predominance of the isomer formed by methylation on the face carrying the largest aryl substituent. In cyanoethylation of structurally similar tricyclic ketones two groups of workers [6,7] report the less hindered as the predominant product, whilst a third group [8] found an excess of the more hindered isomer. Heusler, Ueberwasser, and Wieland [9] draw attention, however, to the known reversibility




(*a*) R = Pr$^i$, (*b*) R = ·CMe:CH$_2$, (*c*) R = ·CHMe·CO$_2$Me.

of Michael-addition alkylation and to the importance of experimental conditions and the nature of the addend [10] in presenting examples of exclusive formation of either isomer. Sarett and his co-workers [11] obtained exclusively the more stable isomer in some examples of substitutive alkylation. Bromination and deuteration preferentially from the more hindered side of an enol which have also been noted and discussed, particularly by Corey and Sneen,[12] disclose a tendency which may be related to examples of alkylation where the more hindered product is obtained.

Of the tetrahydro-*epi*-α-cyperones, m. p. 67° and 108°, noted above, the former, obtained by lithium in liquid ammonia reduction, is regarded as the 4α-methyl-*trans*-ketone (II); the latter, which is resistant to alkali-isomerisation, is therefore the 5 : 10-*cis*-isomer (III) having the 4-methyl substituent in the stable configuration corresponding to the conformation (XVI; R = Pr$^i$, R′ = H). The *cis*- (III) and the *trans*-isomer (II) are formed in the ratio *ca.* 17 : 3 in hydrogenation of the ketone (XI*a*); *inter alia*, the 7α-side-chain will impede *trans*-hydrogenation.

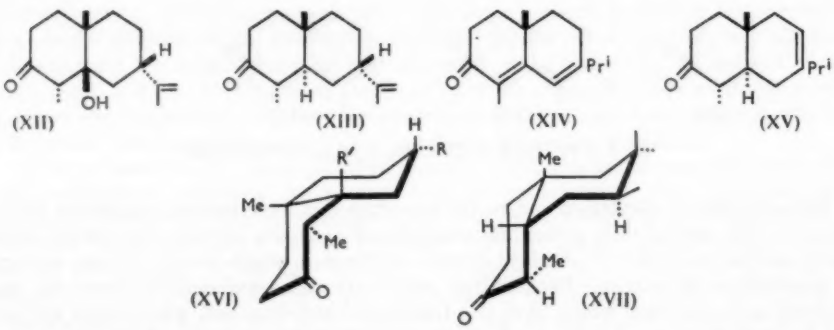
A similar structure (XII) and conformation (XVI; R = ·CMe:CH$_2$, R′ = OH) clearly

[4] Abe, Harukawa, Ishikawa, Miki, and Toga, *J. Amer. Chem. Soc.*, 1953, **75**, 2567; cf. Clemo and McQuillin, *J.*, 1952, 3839.
[5] Johnson, Christiansen, and Ireland, *J. Amer. Chem. Soc.*, 1957, **79**, 1995.
[6] Woodward, Sondheimer, Taub, Heusler, and MacLamore, *ibid.*, 1952, **74**, 4223.
[7] Wieland, Ueberwasser, Anner, and Miescher, *Helv. Chim. Acta*, 1953, **36**, 1231.
[8] Barkley, Knowles, Raffelson, and Thompson, *J. Amer. Chem. Soc.*, 1956, **78**, 4111.
[9] Heusler, Ueberwasser, and Wieland, *Helv. Chim. Acta*, 1957, **40**, 323.
[10] Szpilfogel, Van de Burg, Siegmann, and Van Dorp, *Rec. Trav. chim.*, 1956, **75**, 1043.
[11] Sarett, Johns, Beyler, Lukes, Poos, and Arth, *J. Amer. Chem. Soc.*, 1953, **75**, 2112.
[12] Corey and Sneen, *ibid.*, 1956, **78**, 6269.

represent the ketol previously described [3] in its resistance to base-catalysed dehydration and inversion of the side-chain orientation at a hydrogenation catalyst.[1] Dehydration will involve an increase in compression; the side-chain is already equatorial.

The proportion (11 : 14) of *cis*- (VII) and *trans*-tetrahydrocyperone (VI) formed on hydrogenation of the 7β-substituted natural ketone (V) in ethanol contrasts with the predominantly *cis*-reduction of the 7α-substituted ketone (XI*a*) and illustrates the effect of the 7-substituent on the course of reduction. The 7β-substituted *trans*-tetrahydroketone (VI) has already been described.[1] The *cis*-ketone (VII) has now been obtained by hydrogenation in alkaline ethanol; alkali has been noted [13] to promote *cis*-reduction of steroid analogues. From the properties of these pure ketones the composition of the mixture obtained in neutral alcohol may be estimated.

The predominantly *trans*- and *cis*-reduction of (+)-α-cyperone (V) in neutral and alkaline ethanol respectively is in agreement with the mainly *trans*-reduction of (−)-α-santonin in neutral or acid media,[14,15] and with the reported *cis*-reduction of sodium santoninate [15] (effectively in alkaline solution). Under neutral conditions cholest-4-en-3-one and 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-octahydro-9-methyl-3-oxonaphthalene on the other hand are hydrogenated to *cis*-products.[16,17] The 4-methyl group of the sesquiterpene appears therefore to promote *trans*-reduction. This may arise from the very close proximity of the 4α-methyl and 7α-substituent in the first product (XVII) of 4β : 5β-addition of hydrogen. The reported *trans*-reduction [18] of 4-methylcholest-4-en-3-one is in agreement with this. In alkaline solution intervention of an enol will obviate this effect.



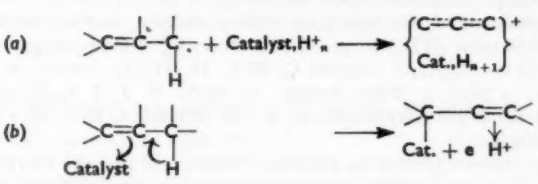

The effect of alkali on the hydrogenation of (+)-*epi*-α-cyperone (I) has also been examined. In neutral alcohol this ketone gives [1] as the major product a *cis*–*trans*-mixture of the 7β-ketones (VII) and (VI), together with a small amount of the uninverted *cis*-7α-ketone (III), accompanied by a minor proportion of the *trans*-isomer (II). The double-bond mobility responsible for inversion at position 7 appears to be impeded in an alkaline medium; under these conditions the principal product of hydrogenation proves to be the *cis*-7α-ketone (III). Hydrogenation of the dihydro-ketone (XIII) in alkaline ethanol similarly led to the uninverted product (II) in place of the 7β-*iso*propyl-ketone (VI) obtained [1] under neutral conditions. The formation of minor amounts of the inverted 7β-products in these experiments cannot, however, be excluded.

[13] See Slomp, Shealey, Johnson, Donia, Johnson, Holysz, Pedersen, Jensen, and Ott, *J. Amer. Chem. Soc.*, 1955, **77**, 1217.
[14] Kovaks, Herout, Horak, and Šorm, *Coll. Czech. Chem. Comm.*, 1956, **21**, 225; Yanagita and Tahara, *J. Org. Chem.*, 1955, **20**, 959; Tahara, *ibid.*, 1956, **21**, 222; Djerassi, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1956, **78**, 6362.
[15] Cocker and McMurry, *J.*, 1956, 4549.
[16] Grasshof, *Z. physiol. Chem.*, 1934, **223**, 249.
[17] Dauben, Rogan, and Blanz, *J. Amer. Chem. Soc.*, 1954, **76**, 6384.
[18] Meakins and Radig, *J.*, 1956, 4679.

(+)-*epi*-α-Cyperone (I) undergoes [1] bond migration to yield (+)-β-cyperone (XIV) when boiled in alcohol with palladised charcoal. The same result has now been obtained in an alkaline medium. We employed ethanolic potassium acetate; the use of alcoholic potassium hydroxide was examined, but not surprisingly, promoted extensive reduction of the carbonyl group. (+)-Dihydro-*epi*-α-cyperone (XIII), which undergoes a similar catalysed bond migration,[1] has now been shown also to lead to the same product, a ketone (XV), $[\alpha]_{4461}$ −72°, in both neutral alcohol and in ethanolic potassium acetate. This isomerised ketone (XV) and the parent (XIII) gave the same tetrahydro-ketone (VI) on hydrogenation.

In alcoholic alkali, hydrogenation of the 4 : 5-double bond of the enone system in both ketones (I) and (II) was found to be very much faster than that of the isolated 11 : 12-double bond. This enabled us to obtain the otherwise difficultly accessible *cis*-dihydro-ketones (IV) and (VIII); this method of selective hydrogenation may prove more widely useful.

Bream, Eaton, and Henbest [19] have discussed a number of examples of catalysed migration of olefinic bonds in steroids and have summarised the geometrical requirements of the reaction in a mechanism (*a*) involving acid catalysis. This has analogies in the known hydrogenolysis of allyl alcohols, with or without accompanying bond migration.[20, 21] Our previous results, obtained in neutral alcohol, were rationalised [1] in terms of a mechanism (*b*), and the present work was in part an attempt to distinguish between these alternatives. With this aim we have therefore examined the hydrogenation of (+)-*epi*-α-cyperone (I), also in acidified ethanol, which in a very rapid reaction gave the same mixture of 7-inverted and 7-uninverted products as in neutral alcohol, and in benzene which gave the mixture of 7-inverted ketones (VI) and (VII) in a very slow reaction.




These results indicate that hydrogenation and migration of an olefinic double bond are apparently proton-catalysed but not proton-dependent processes, to which, on present evidence, (*a*), (*b*), or other mechanisms may apply in different conditions.

In this work we have employed the palladised charcoal " catalyst-d " of Linstead and Thomas [22] which was washed until it gave a neutral reaction in water.

## Experimental

[α] are for solutions in chloroform.

(+)-3-*Oxo*-4 : 5 : 7β(H)-*eudesmane* (III) *and Comparison with the Material of Bradfield, Jones, and Simonsen.*—This ketone is best prepared by hydrogenation of (+)-3-oxo-7β-(*H*)-eudesm-4-ene (XI*a*) as previously described.[1] The hydrogenation product (from alcohol with palladised charcoal) was obtained by chromatography and crystallisation (from pentane) as fractions showing apparently sharp m. p.s between 89° and 100°. Repeated crystallisation from pentane gave needles, m. p. 108°, unchanged by further crystallisation, $[\alpha]_{4461}$ +24·0° (*c* 4·5) (Found: C, 80·8; H, 11·85. Calc. for $C_{15}H_{26}O$: C, 81·1; H, 11·7%). The 2 : 4-*dinitrophenylhydrazone* formed orange prisms, m. p. 123° from ethanol (Found: C, 62·5; H, 7·6. $C_{21}H_{30}O_4N_4$ requires C, 62·7; H, 7·5%). The *oxime* described previously [1] as an oil was obtained with m. p. 77—78° (from aqueous methanol), $[\alpha]_{4461}$ −68·5° (*c* 2·94) (Found: C, 75·8;

[19] Bream, Eaton, and Henbest, *J.*, 1957, 1974.
[20] Dauben and Hance, *J. Amer. Chem. Soc.*, 1955, **77**, 2451.
[21] Henbest and Jones, *J.*, 1948, 1798.
[22] Linstead and Thomas, *J.*, 1940, 1127.

XUM

H, 11·5. $C_{15}H_{27}ON$ requires C, 76·0; H, 11·4%). The semicarbazone formed prisms, m. p. 213—214° (decomp.) from aqueous methanol, $[\alpha]_{5461}$ −16·0° (*c* 0·9) (Found: C, 68·75; H, 10·7. Calc. for $C_{16}H_{29}ON_3$: C, 68·8; H, 10·4%). The semicarbazone obtained by Bradfield, Jones, and Simonsen,[2] kindly made available by Dr. L. N. Owen, had m. p. 210° (decomp.), $[\alpha]_{5461}$ −13·0° (*c* 0·8), and showed no depression of the m. p. on admixture with our sample.

(−)-3-*Oxo*-4 : 7β(H)-*eudesmane* (II).—After removal of the crystalline ketone, m. p. 108° (above), the remaining material was distilled to give an oil, b. p. 90°/0·1 mm. [0·172 g. from 0·8 g. of (+)-dihydro-*epi*-α-cyperone], $[\alpha]_{5461}$ +2·9° (*c* 4·8). This material gave a 2 : 4-dinitrophenylhydrazone, m. p. 189—194° raised by crystallisation from ethyl acetate to 222—224° (Found: C, 62·85; H, 7·7%), and did not depress the m. p. of the 2 : 4-dinitrophenylhydrazone, m. p. 222—223°, reported by Bradfield, Jones, and Simonsen or that of the derivative of authentic (−)-3-oxo-4 : 7β(*H*)-eudesmane (II) prepared earlier.[1]

*Attempted Isomerisation of* (+)-3-*Oxo*-4 : 5 : 7β(H)-*eudesmane* (III).—This ketone, m. p. 108° (50 mg.), in ethanol (4 c.c.) with potassium hydroxide (0·5 g.) in water (1 c.c.) was recovered (43 mg.; m. p. and mixed m. p. 108°) after 6 hours' refluxing under nitrogen.

*Hydrogenation of* (+)-α-*Cyperone in Alkaline Ethanol.*—(i) (+)-α-Cyperone (1 g.) in ethanol (20 c.c.) containing potassium hydroxide (0·4 g.), shaken with palladised charcoal, absorbed 1 mol. of hydrogen during 0·5 hr. The product, b. p. 95°/0·1 mm., $n_D^{20}$ 1·4980, [α] +28·8°, showed no absorption due to an enone group in the ultraviolet or infrared spectrum. Strong absorption at 890 cm.$^{-1}$ indicated, however, that the *iso*propenyl group was intact. It was purified *via* the *oxime* which was obtained with m. p. 96° (from methanol), [α] +89·5° (*c* 2·8) (Found: C, 76·45; H, 10·5. $C_{15}H_{25}ON$ requires C, 76·6; H, 10·6%). Hydrolysis by the previously described method[3] gave (+)-3-*oxo*-4α : 5β(H)-*eudesm*-11-*ene* (VIII), b. p. 95°/0·1 mm., $n_D^{20}$ 1·5000, $[\alpha]_{5461}$ +29·1° (*c* 9·1) (Found: C, 82·0; H, 11·3. $C_{15}H_{24}O$ requires C, 81·8; H, 10·9%). The 2 : 4-*dinitrophenylhydrazone* formed needles (from ethanol), m. p. 157° (Found: C, 62·7; H, 7·2. $C_{21}H_{28}O_4N_4$ requires C, 63·0; H, 7·0%).

(ii) Further hydrogenation of this substance with palladised charcoal in alcohol afforded (+)-3-*oxo*-4α : 5β(H)-*eudesmane* (VII), b. p. 95°/0·1 mm., $n_D^{20}$ 1·4894, $[\alpha]_{5461}$ +30·4° (*c* 2·9) (Found: C, 81·4; H, 12·0. $C_{15}H_{26}O$ requires C, 81·1; H, 11·7%) [*oxime*, m. p. 108° (from aqueous methanol), [α] +28·8° (*c* 2·26) (Found: C, 75·6; H, 11·7. $C_{15}H_{29}ON$ requires C, 75·95; H, 11·4%); 2 : 4-*dinitrophenylhydrazone*, m. p. 155° (Found: C, 62·9; H, 7·2. $C_{21}H_{32}O_4N_4$ requires C, 62·7; H, 7·5%)].

*Hydrogenation of* (+)-epi-α-*Cyperone in Alkaline Ethanol.*—(i) (+)-*epi*-α-Cyperone (0·515 g.) in 2% ethanolic potassium hydroxide (25 c.c.) with palladised charcoal (300 mg.) absorbed 1 mol. of hydrogen in 5 hr. The product crystallised and was chromatographed on alumina, to give (+)-3-*oxo*-4 : 5 : 7β(H)-*eudesm*-11-*ene* (IV), as needles, m. p. 92—93° (from pentane), $[\alpha]_{5461}$ +26·0° (*c* 3·94) (Found: C, 81·9; H, 11·1. $C_{15}H_{24}O$ requires C, 81·8; H, 10·9%). The *oxime* formed plates, m. p. 107° (from aqueous methanol), $[\alpha]_{5461}$ −73·2° (*c* 4·0) (Found: C, 76·7; H, 10·85. $C_{15}H_{25}ON$ requires C, 76·6; H, 10·6%); the 2 : 4-*dinitrophenylhydrazone* had m. p. 194° (from ethyl acetate–ethanol; after chromatography on alumina) (Found: C, 62·75; H, 7·05. $C_{21}H_{28}O_4N_4$ requires C, 63·0; H, 7·0%).

(ii) In a similar experiment in 10% alcoholic potassium hydroxide, (+)-*epi*-α-cyperone (0·4 g.) was hydrogenated to saturation in 120 hr. The product, on chromatography, gave the crystalline mixture of *cis*- and *trans*-7α-*iso*propyl-ketones (II) and (III), m. p. 97°, $[\alpha]_{5461}$ +21·2° (0·11 g.).

*Hydrogenation of* (+)-epi-α-*Cyperone in Acid Ethanol.*—The ketone (0·4 g.) in ethanol (20 c.c.) containing 1 drop of concentrated hydrochloric acid and palladised charcoal absorbed 2 mols. of hydrogen in 24 min. The product, by chromatography, gave a little of the crystalline mixture, m. p. 97—98°, of the *cis*- and *trans*-7α-*iso*propyl-ketones (II) and (III), and fractions eluted later gave the oxime, m. p. 117°, of the mixture of *cis*- and *trans*-7β-*iso*propyl-ketones (VI) and (VII) undepressed on admixture with the specimen prepared previously.[1]

*Hydrogenation of* (+)-epi-α-*Cyperone in Benzene.*—The ketone hydrogenated in benzene with palladised charcoal absorbed a little less than 2 mols. in 3 days. Chromatography removed a little unreduced material to give a fully reduced product, $n_D^{20}$ 1·4864, $[\alpha]_{5461}$ +5·0° (*c* 6·3). Further chromatography gave no crystalline material, but the oxime of the mixture of *cis*- and *trans*-7β-*iso*propyl-ketones (VI) and (VII), m. p. 117°, $[\alpha]_{5461}$ −63° (*c* 2·6), could be isolated in good yield.

*Isomerisation of* (+)-epi-α-*Cyperone in Ethanolic Potassium Acetate.*—(+)-*epi*-α-Cyperone

(0·15 g.) in ethanol (9 c.c.) and water (1 c.c.) with potassium acetate (1 g.) was heated under reflux with palladised charcoal (0·1 g.) in nitrogen for 20 hr. The product, $n_D^{20}$ 1·5564, $[\alpha]_{5461}$ +583° (*c* 3·96), afforded (+)-β-cyperone oxime, m. p. and mixed m. p. 139°, $[\alpha]_{5461}$ +346° (*c* 1·06), in good yield.

*Isomerisation of* (+)-trans-4 : 5-*Dihydro*-epi-α-*cyperone in Ethanol and in Ethanolic Potassium Acetate.*—(i) The ketone (0·235 g.) in ethanol (10 c.c.) was refluxed with 20% palladised charcoal (250 mg.) for 100 hr., and on recovery gave a pale yellow ketonic oil, b. p. 90°/0·1 mm. Chromatography on alumina and elution with light petroleum gave the dihydro-ketone (XV), b. p. 90°/0·1 mm., $n_D^{20}$ 1·4990, $[\alpha]_{5461}$ −72° (*c* 6·0), which showed no infrared absorption due to $>C{:}CH_2$ (Found: C, 82·1; H, 10·9. $C_{15}H_{24}O$ requires C, 81·8; H, 10·9%). The 2 : 4-*dinitrophenylhydrazone* formed yellow needles, m. p. 154—155° (from ethanol), $[\alpha]_D$ −214° (*c* 1·9) (Found: C, 62·8; H, 7·4. $C_{21}H_{28}O_4N_4$ requires C, 63·0; H, 7·0%) (cf. ref. 1).

The isomerised ketone (XV) (37 mg.) in ethanol absorbed 1 mol. of hydrogen in 4·5 hr., to give a product which was converted directly into the oxime, m. p. and mixed m. p. 117—118°, $[\alpha]_{5461}$ −124·4° (*c* 2·2), of the tetrahydro-ketone (VI), identical with that obtained by direct reduction of the ketone (XIII) without prior isomerisation.[1]

(ii) The ketone (75 mg.) was refluxed with catalyst in aqueous ethanolic potassium acetate, as in the case of (+)-*epi*-α-cyperone. The product, $n_D^{20}$ 1·4977, $[\alpha]_{5461}$ −75° (*c* 1·3), had the same infrared spectrum as the ketone (XV) obtained in neutral ethanol.

*Reduction of* (+)-trans-4 : 5-*Dihydro*-epi-α-*cyperone in Alkaline Solution.*—The ketone (0·148 g.) in 2% ethanolic potassium hydroxide (20 c.c.) with 20% palladised charcoal (0·3 g.) absorbed 1 mol. of hydrogen in 4 days. The product, b. p. 95°/0·2 mm., $n_D^{20}$ 1·4970, $[\alpha]_{5461}$ −40·7° (*c* 2·73), showed no $>C{:}CH_2$ absorption. It gave a 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 223° (from ethyl acetate), identical with that of the tetrahydro-ketone (II). The mother-liquors, on chromatography, gave a 2 : 4-dinitrophenylhydrazone, m. p. 157°, $[\alpha]_D$ −163° (*c* 0·1), showing no depression on admixture with the 2 : 4-dinitrophenylhydrazone of the dihydro-ketone (XV). The low rotation indicates that this material probably contains some of the derivative [1] of the tetrahydro-ketone (VI) (2 : 4-dinitrophenylhydrazone, $[\alpha]_D$ −126°).

One of us (R. H.) thanks the Department of Scientific and Industrial Research for an award.

King's College, Newcastle upon Tyne, 1. [*Received, September 27th*, 1957.]

---

## 237. *The Alkaline Degradation of Polysaccharides. Part III.* Action of Sodium Hydroxide on Amylose.*

By G. Machell and G. N. Richards.

The action of 0·5N-sodium hydroxide at 100° on amylose is of two main types: "degradation" producing mainly D-gluco*iso*saccharinic, formic, and lactic acid; and a "stopping" reaction affording alkali-stable amylose probably bearing terminal D-gluco*meta*saccharinic acid units. The analogy with the similar degradation of cellulose is discussed.

Much of the earlier work on the alkaline degradation of starch and its amylose component was concerned with attempts to relate the extent of degradation to the initial molecular weight of the material. This work led to the development of the "alkali-number" determination,[1] which is a measure of the amount of acid formed when starch or amylose is degraded in alkali under standard conditions. The alkali number is related to the initial molecular weight provided the degradation commences only at reducing glucose end-units present in the original material. However, the method is particularly sensitive to traces of oxygen, which cause a random scission of the polysaccharide,[2] with possible production of new reducing end-groups. Additional interest in the alkaline degradation

* Part II, *J.*, 1957, 4500.

[1] Schoch and Jensen, *Analyt. Chem.*, 1940, **12**, 531.

[2] Bottle, Gilbert, Greenwood, and Saad, *Chem. and Ind.*, 1953, 541.

of starch arises from the possibility of modification of the polysaccharide during alkaline extraction.

Bottle and Gilbert [3] examined the effect of boiling, oxygen-free, aqueous sodium hydroxide on potato amylose of D.P. 415 and found that the degradation ceased when an average of 230 glucose residues per chain had been degraded. This cessation of attack was ascribed to a termination reaction, *i.e.*, conversion, during the degradation of a reducing glucose end-unit into an alkali-stable group. No suggestion was made as to the nature of the latter, and this interpretation was in conflict with that of Taylor and Salzmann [4] who considered that amylose contained two fractions, one completely degraded by, and the other stable to, alkali. Bottle and Gilbert's observations can be related to the results obtained from a recent study of the action of alkali on the chemically similar cellulose under similar conditions.[5] In this case also, the progressive stepwise degradation from the reducing end-group is arrested by a reaction in which a terminal reducing glucose unit is rearranged to an alkali-stable group.

The material used in the present work was cold-alkali extracted potato amylose hydrolysed in acid to D.P. *ca.* 450; the results of the degradation of this material in sodium hydroxide are shown in Table 1, and agree well with Bottle and Gilbert's finding.[3] It is evident that the degradation has virtually ceased after about 20 hr., when approximately 60% of the amylose has been degraded, yielding *ca.* 1·4 equiv. of acid per glucose residue removed. Schoch and Jensen [1] had stated that the degradation products formed under such conditions included formic, acetic, and lactic acid and pyruvaldehyde, although they gave no supporting evidence. A preliminary examination [6] of the major acidic products has now been extended, these products being examined by paper chromatography and, where possible, identified by isolation and preparation of derivatives. The proportions of the main products have also been determined, and all of these results are summarised in Table 2. For comparison, the yields of acids obtained from cellulose under similar conditions [5a] have been included.

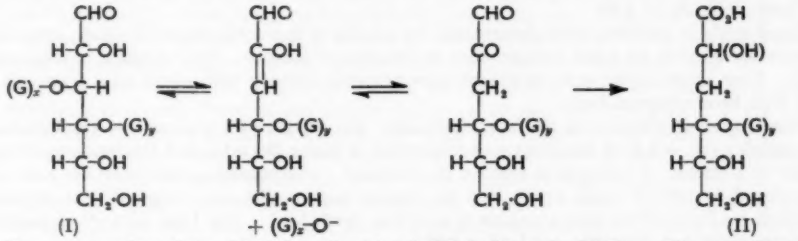
The alkali-stable polysaccharide obtained from the alkaline degradation of amylose was hydrolysed in dilute acid, and the products separated into acidic and neutral fractions by an ion-exchange procedure.[7] In the neutral products were found glucose and traces of maltose and a disaccharide reversion product. Rigorous identification of the acidic, alkali-stable end-unit was ruled out by the small amount isolated, but paper chromatography indicated the presence of approximately equal amounts of α- and β-D-gluco-*meta*saccharinic acid.

The nature and proportions of both the acidic degradation products and the alkali-stable polysaccharide obtained from the alkaline degradation of amylose are, as expected, similar to those of the analogous products from the cellulose. It follows, therefore, that in the alkaline degradation of amylose, as for cellulose, there are two main types of reaction: " degradation " giving mainly D-gluco*iso*saccharinic, formic, and lactic acid, and the " stopping " reaction in which a terminal glucose unit rearranges to D-gluco*meta*saccharinic acid. Mechanisms proposed are the same as those given [5] for cellulose.

It has been suggested, however, that the results of certain enzymatic degradations of amylose can only be explained by assuming the presence of branches linked to the main amylose chain, possibly by 1 : 3-β-glycosidic linkages.[8] On the basis of experiments with simpler related compounds,[9] the presence of 1 : 3-linked branches would lead to rearrangement in alkali, to D-gluco*meta*saccharinic acid, of the glucose units bearing such branches when these units became exposed during the course of the degradation. This situation is

[3] Bottle and Gilbert, *Chem. and Ind.*, 1954, 1201.
[4] Taylor and Salzmann, *J. Amer. Chem. Soc.*, 1933, **55**, 264.
[5] (*a*) Richards and Sephton, *J.*, 1957, 4492; (*b*) Machell and Richards, *J.*, 1957, 4500.
[6] Kenner and Richards, *Chem. and Ind.*, 1954, 1483.
[7] Machell, *J.*, 1957, 3389.
[8] Peat, Thomas, and Whelan, *J.*, 1952, 722; Peat and Whelan, *Nature*, 1953, **172**, 494; cf. Bird and Hopkins, *ibid.*, p. 493.
[9] Kenner and Richards, *J.*, 1954, 3277.

depicted in the annexed scheme. However, the analogy with cellulose, in which such 1 : 3-linked branches are very unlikely, suggests that at least part of the "stopping" reaction involves rearrangement at an unsubstituted reducing end-unit.




(I) = main amylose chain of D.P. (y + 1) with a 1 : 3-linked branch of D.P. x. (II) = resulting alkali-stable amylose.

The results obtained from the alkaline degradation of amylose and cellulose, particularly the relative yields of D-gluco*iso*saccharinic, formic, and lactic acid, should be paralleled in the alkaline degradation of 1 : 4-linked glucans in general and should also be applicable to other polyhexoses, such as mannans. It would be expected that a study of the alkaline degradation of amylopectin, in particular the effect on D.P., would help in their structural investigation.[10]

TABLE 1. *Degradation of amylose in* 0·5N-*sodium hydroxide at* 100°.

| Time (hr.) | Acid formed (milliequiv.) | Decrease in A.V. at $\lambda_{max.}$ (%) | $\lambda_{max.}$ (mμ) | Time (hr.) | Acid formed (milliequiv.) | Decrease in A.V. at $\lambda_{max.}$ (%) | $\lambda_{max.}$ (mμ) |
|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 637 | 7 | 0·214 | 53·3 | 635 |
| 0·5 | 0·096 | 26·9 | 637 | 21 | 0·292 | 62·8 | 632 |
| 2 | 0·192 | 48·0 | 637 | 40 | 0·316 | 64·7 | 632 |

A.V. = absorption value of iodine-stained polysaccharide residue.

TABLE 2. *Acids from degradation of amylose in* 0·5N-*sodium hydroxide at* 100°.

| Acid | $R_L$ value (solvent *a*) | Yield (% total equivs.) from amylose | from cellulose |
|---|---|---|---|
| α,β-D-Gluco*iso*saccharinic | 0·14 (acid) | *ca.* 23 | *ca.* 31 |
| | 0·55 (lactone) | | |
| Supposed dihydroxybutyric | 0·59 (acid) | — | — |
| | 1·04 (lactone) | | |
| Supposed αβ-dihydroxy-α-methylpropionic | 0·69 | — | — |
| Glycollic | 0·74 | — | — |
| Lactic | 1·00 | 6 | 6 |
| Lactyl-lactic | 1·23 | — | — |
| Formic | — | 35 | 33 |
| Unknown | 0·47, 0·51, 0·81 | — | — |

## EXPERIMENTAL

Amylose was kindly provided by Mrs. L. M. Gilbert; it was prepared by cold-alkali fractionation of potato starch,[11] followed by hydrolysis of the amylose fraction with 0·002N-hydrochloric acid at 100° for 20 min. under nitrogen, and isolation as the butan-1-ol complex.[12] From measurements of the hydrolysis constant,[13] the D.P. of the hydrolysed material was estimated as *ca.* 450.

The following solvents and sprays were used for paper chromatography with Whatman No. 1 paper at 25°: solvents; (*a*) [14] ethyl acetate–acetic acid–water (10 : 1·3 : 1);

[10] Cf. Greenwood, *Adv. Carbohydrate Chem.*, 1956, **11**, 335.
[11] Baum and Gilbert, *J. Colloid Sci.*, 1956, **11**, 428.
[12] Lansky, Kooi, and Schoch, *J. Amer. Chem. Soc.*, 1949, **71**, 4066.
[13] Baum and Gilbert, unpublished work.
[14] Richtzenhain and Moilanen, *Acta Chem. Scand.*, 1954, **8**, 704.

(*b*) ethanol–ammonia (*d* 0·88)–water (85 : 1 : 14); (*c*) ethyl acetate–pyridine–water (8 : 2 : 1); (*d*) butan-1-ol–ethanol–acetic acid–water (45 : 5 : 1 : 49). Sprays; (*a*) [15] B.D.H. 4·5 Indicator; (*b*) [16] hydroxylamine–ferric chloride; (*c*) [17] sodium periodate–potassium permanganate; (*d*) [18] B.D.H. 4·5 Indicator buffered with citric acid; (*e*) [19] silver nitrate–sodium hydroxide. For lactic acid, $R_L = 1·00$.

Total acids in solution were determined by adding a two-fold excess of alkali, keeping the mixture for 30 min. at room temperature to decompose lactones, and titrating it with acid to pH 9. Free acids in the same solutions were titrated directly with alkali to a transient end-point with bromothymol-blue.

*Degradation of Amylose in Sodium Hydroxide: Quantitative Experiments.*—Amylose–butan-1-ol complex (*ca.* 0·5 g. of amylose) was suspended in water (80 ml.), and the suspension heated at 100° in a stream of nitrogen to remove the butanol. The resulting clear solution was cooled, and diluted to 100 ml. with water, and an aliquot portion (10 ml.) evaporated to dryness as described by Bottle,[20] to give a residue of amylose (0·0544 g.). The blue value [21] measured by a Unicam spectrophotometer was 1·36 at 680 mμ.

Further 10 ml. portions of the same solution were transferred to Polythene ampoules, which were each placed inside a glass tube partly filled with water. Oxygen was removed by a stream of nitrogen, which was continued while oxygen-free N-sodium hydroxide (10 ml.) was added, and the assembly was immersed in a boiling-water bath. After varying times, the reaction was arrested by cooling with ice, and the resulting solution was run through a column of Amberlite IR-120(H) resin (25 ml.) to remove sodium ions. The total acid in the effluent was determined by titration of an aliquot portion, and the absorption value [21] (A.V.) of the iodine stain of the residual amylose on a second portion. Results are given in Table 1.

*Soluble Products from the Degradation of Amylose in Sodium Hydroxide.*—(a) *Qualitative.* A suspension of amylose–butan-1-ol complex (*ca.* 20 g. of amylose) in water was freed from butanol by steam-distillation under nitrogen. The volume of the suspension was then adjusted to 250 ml., and oxygen removed by a stream of nitrogen. Oxygen-free N-sodium hydroxide (250 ml.) was added, and the clear solution heated in a boiling-water bath for 20 hr. The resulting dark brown solution was cooled in ice, diluted to 3 l., and run through a column of Amberlite IR-120(H) resin (300 ml.) to remove sodium ions. Alkali-stable amylose in the acidic effluent was precipitated as its complex with butan-1-ol, and the complex recovered in the centrifuge, washed thoroughly with water previously saturated with butan-1-ol, and retained for later examination.

The acidic centrifugate and initial washings were combined (4 l.), distilled at 20 mm. with the bath temperature at 40—50°, and the distillate collected at 0°. Distillation was arrested when *ca.* 3 l. of distillate had collected; the latter was made 2N with respect to hydrochloric acid, and a saturated solution of 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid (200 ml.) added. Slow deposition of a yellow solid took place and, after one month, this was collected. Crystallisation of this material from anisole afforded dark red crystals (*ca.* 40 mg.) which decomposed at *ca.* 265°, and were not further investigated. The distillation was continued to give a syrupy residue, to which were added two successive portions of water (30 ml.), each addition being followed by distillation to a syrup. An aliquot portion of the distillate (350 ml. from 1 l.) was neutralised with sodium hydroxide, and the solution of sodium salts evaporated to small bulk (5 ml.) under reduced pressure. From this concentrate was prepared *p*-bromophenacyl formate, m. p. and mixed m. p. 134—135° (from acetone–light petroleum).

The residue of non-volatile acids remaining from the above distillation was dried to constant weight (4·02 g.) over phosphoric oxide *in vacuo*. Paper chromatography of the acid mixture was carried out with solvent *a*, and for comparison a standard mixture containing D-glucoisosaccharinic acid and its lactone, glycollic and lactic acid. Spray *a* developed components corresponding to the following acids: α,β-D-glucoisosaccharinic ($R_L$ 0·14), dihydroxybutyric ($R_L$ 0·59), αβ-dihydroxy-α-methylpropionic ($R_L$ 0·69), glycollic ($R_L$ 0·74), lactic ($R_L$ 1·00), and lactyl-lactic ($R_L$ 1·23). In addition there were traces of unknown acids having $R_L$ 0·47, 0·51,

[15] Nair and Muthe, *Naturwiss.*, 1956, **43**, 106.
[16] Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 5859.
[17] Lemieux and Bauer, *Analyt. Chem.*, 1954, **26**, 920.
[18] Cf. Kennedy and Barker, *ibid.*, 1951, **23**, 1033.
[19] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[20] Bottle, *Chemist-Analyst*, 1956, **45**, 82.
[21] Bourne, Haworth, Macey, and Peat, *J.*, 1948, 924.

and 0·81. Application of spray *b* revealed components corresponding to D-gluco*iso*saccharinolactone ($R_L$ 0·55) and dihydroxybutyrolactone ($R_L$ 1·04). Use of spray *c* indicated that D-gluco*iso*saccharinic acid and its lactone were the main constituents of the non-volatile acids.

An aqueous solution (250 ml.) of the residue of non-volatile acids was found by titration to contain 5·75 milliequiv. of free acids and 24·75 milliequiv. of lactones. This solution was heated to 70—80° and stirred with an excess of calcium hydroxide to decompose lactones and form the corresponding calcium salts. Excess of lime was removed by filtration, and the filtrate saturated with carbon dioxide, boiled for 5 min., and again filtered. The solution of calcium salts was decolorised with charcoal and evaporated to *ca.* 20 ml. After storage at 4° for 3 days, the concentrate deposited a white solid (0·4 g.) which recrystallised from boiling water. The purified salt was heated with an excess of Amberlite IR-120(H) resin at 70° for 1 hr. to liberate the acid and promote its lactonisation, the latter process being further facilitated by evaporating the solution and drying the residue over phosphoric oxide *in vacuo*. Crystallisation of the dried syrup (0·11 g.) from ethyl acetate gave α-D-gluco*iso*saccharinolactone, m. p. and mixed m. p. 93—94°. Paper chromatography of the lactone in solvent *a*, with sprays *b* and *c* gave a single spot, $R_L$ 0·55; in solvent *b* and with sprays *c* and *d*, the corresponding ammonium salt prepared from the lactone gave a single spot, $R_L$ 0·71.

(b) *Quantitative.* Amylose (*ca.* 1 g.) was treated with 0·5N-sodium hydroxide (50 ml.) at 100° for 30 min. in the absence of oxygen, as previously described. The cooled mixture was then freed from sodium ions by passing it through a column of Amberlite IR-120(H) resin (50 ml.), and stored at 4° overnight. Retrograded amylose was then removed by filtration, and the filtrate, which still contained amylose, was stirred with De-Acidite FF (micro-bead; 2% cross-linked) carbonate (5 g.) for 24 hr.[7] The resin was transferred to a column and washed with water (500 ml.), and the filtrate and washings containing the amylose and any other neutral products were rejected.

Sorbed acids were eluted from the resin with N-ammonium carbonate (100 ml.), and the eluate evaporated to dryness under reduced pressure to decompose the excess of eluant. The residue of ammonium salts was taken up in water (50 ml.) and passed through a column of Amberlite IR-120(H) resin (10 ml.). By titration of an aliquot portion of the effluent, the total acid present was found to be 2·16 milliequiv. Lactic acid in this solution was determined by Hullin and Noble's method [22] (the lime treatment being omitted); formic acid, other volatile acids, and D-gluco*iso*saccharinic acid were determined as described earlier.[5a] The results (as percentages of acid equivalents) were: formic acid, 35%; other volatile acids, 3%; lactic acid, 6%; and D-gluco*iso*saccharinic acid, *ca.* 23%.

*Acidic Hydrolysis of Alkali-stable Amylose and Identification of Products.*—The alkali-stable amylose–butan-1-ol complex (*ca.* 7·5 g. of amylose) obtained in an earlier experiment was freed from butan-1-ol as described, and suspended in N-hydrochloric acid (200 ml.). After 2 hr. at 100° in a stream of nitrogen, all the solid had dissolved, leaving a pale brown solution, which was decolorised with charcoal. The solution was then substantially freed from hydrochloric acid by shaking it with methyldi-*n*-octylamine [23] (51 g., 0·2 mole) in chloroform (500 ml.), and the aqueous layer was separated, washed with chloroform, and concentrated to 30 ml. at 40°/20 mm. Cations were removed from the concentrate by passage through a column of Amberlite IR-120(H) resin (10 ml.), and the acidic effluent was neutralised with silver carbonate. The small precipitate of silver chloride was removed and silver ions removed from the filtrate by treatment with Amberlite IR-120(H) resin (10 ml.) in a column. A slightly acid solution (pH 3) resulted, and this was stirred with De-Acidite FF (micro-bead; 2% cross-linked) carbonate (5 g.) for 24 hr. to sorb the acids and lactones. The resin was then transferred to a column, in which it was washed with water (500 ml.), and the filtrate and washings were evaporated to a syrup under reduced pressure. After the syrup had been dried to constant weight (7·3 g.) over phosphoric oxide *in vacuo*, it was examined by paper chromatography in solvent *c*. Applications of spray *a* indicated that the material consisted of glucose ($R_F$ 0·30) with traces of maltose ($R_F$ 0·18) and a substance of $R_F$ 0·12. The latter corresponded to isomaltose and gentiobiose, which would be expected to be formed by reversion during the acid hydrolysis.[24]

Acids were eluted from the De-Acidite resin with N-ammonium carbonate (100 ml.), and the

[22] Hullin and Noble, *Biochem. J.*, 1953, **55**, 289.
[23] Smith and Page, *J. Soc. Chem. Ind.*, 1948, **67**, 48.
[24] Thompson, Anno, Wolfrom, and Inatome, *J. Amer. Chem. Soc.*, 1954, **76**, 1309; E. E. Bacon and J. S. D. Bacon, *Biochem. J.*, 1954, **58**, 396.

XUM

eluate freed from ammonium ions as described in the previous experiment. Titration of an aliquot part of the resulting acid solution revealed the presence of 0·18 milliequiv. of total acid, but tests showed that inorganic acids including hydrochloric and sulphuric acids were present. Paper chromatography of this acid solution in solvent *a* with sprays *b* and *e* indicated that the main constituents of the mixture were probably α- and β-D-gluco*meta*saccharinolactone having $R_F$ 0·38 and 0·32 respectively. There was a small amount of a further unidentified lactone with $R_F$ 0·21. With solvent *d* and sprays as above, the α- and β-D-gluco*meta*saccharinolactone had $R_F$ 0·40 and 0·34 respectively, and the unknown lactone $R_F$ 0·19. The last could be D-glucosyl-D-gluco*meta*saccharinolactone present as a result of either incomplete hydrolysis or condensation of D-glucose with the lactone during the isolation.[25] Further investigation of these hydrolysis products was precluded by the small amount of material available.

The authors are grateful to Dr. G. A. Gilbert for helpful discussion. This work forms part of the programme of fundamental research undertaken by the Council of the British Rayon Research Association.

THE BRITISH RAYON RESEARCH ASSOCIATION,
HEALD GREEN LABORATORIES,
WYTHENSHAWE, MANCHESTER, 22. [*Received, October 21st*, 1957.]

[25] Aspinall, Carter, and Los, *J.*, 1956, 4807.

---

## 238. *The Alkaline Degradation of Polysaccharides. Part IV.* Monosaccharide Analogues of Periodate Oxycellulose.*

By D. O'MEARA and G. N. RICHARDS.

A study of the products of alkaline degradation of certain periodate-oxidised monosaccharides suggests that the degradation occurs predominantly by scission of the carbon–oxygen linkage in the β-position with respect to the aldehyde groups. Subsequent rearrangements of the products probably yield a molecule of glycollic acid from each scission of this type. In certain circumstances an intramolecular Cannizzaro rearrangement can occur in the periodate-oxidation product. The analogy with periodate oxycellulose is discussed.

OXIDISED celluloses which contain carbonyl groups are known to undergo chain scission by alkali and this effect has been interpreted by various workers in terms of alkaline hydrolysis of glucosides[1] and acetals,[3] keten acetals,[2] and carbonate esters,[3b] and of β-alkoxycarbonyl elimination.[4] In each case similar arguments could equally well be applied to oxidised amylose.[5] However, the general effect of alkaline elimination of an alkoxyl group from the β-position to a carbonyl group has been proved for simpler compounds such as the *O*-substituted hexoses.[6] In order to extend such an analogy to an oxidised polysaccharide it is necessary to introduce a single type of oxidised group into a chemically pure polysaccharide and a specific oxidant is therefore required. Such a case is periodate oxycellulose. As a preliminary, and in order to develop techniques, we have first considered analogues of low molecular weight.

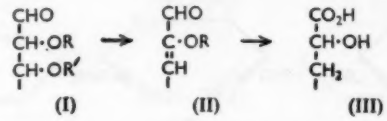
For periodate oxycellulose we assume that alkaline degradation will not appreciably affect secondary cyclic systems resulting from internal acetal formation by the aldehyde

* Part III, preceding paper.

[1] Davidson, *J. Text. Inst.*, 1938, **29**, T 195.
[2] Pacsu, *Text. Res. J.*, 1945, **15**, 354.
[3] (*a*) Head, *J. Text. Inst.*, 1947, **38**, T 389; (*b*) Kaverzneva, Ivanov, and Salova, *Bull. Acad. Sci.* U.S.S.R., 1952, 681.
[4] Haskins and Hogsed, *J. Org. Chem.*, 1950, **15**, 1264; Corbett, Kenner, and Richards, *Chem. and Ind.*, 1953, 154; Kenner, *ibid.*, 1955, 727.
[5] Cf. Anderson, Greenwood, and Hirst, *J.*, 1955, 225; Hofreiter, Alexander, and Wolff, *Analyt. Chem.*, 1955, **27**, 1930.
[6] Kenner and Richards, *J.*, 1957, 2916, and earlier work.

XUM

groups.[7] The structure of an oxidised unit (XIV) is therefore such that, although β-alkoxycarbonyl groupings are present (*a*), the α-hydroxycarbonyl grouping is absent. Now work on 2 : 3-di-*O*-methyl-D-glucose [8] indicates that the normal alkaline degradation of a β-alkoxycarbonyl system (I) will only proceed to completion when the product (II) can undergo further reaction, *e.g.*, to produce a saccharinic acid (III). The latter reaction is evidently dependent on the nature of the group R and probably only occurs readily, as



(I) (II) (III)

shown, when R = H. In such cases (*i.e.*, β-alkoxycarbonyl-α-hydroxy systems), the indications are that the reaction sequence (I) ⟶ (III), particularly in the presence of calcium ions, proceeds almost to completion. In the case of 2 : 3-di-*O*-methyl-D-glucose however, where R = R′ = Me, the product (II) was evidently stable in dilute alkali at room temperature and the acid (III) was not produced under these conditions.

Suitable monosaccharide analogues of periodate oxycellulose must therefore contain substituents which replace the groups adjacent to the oxidised unit in (XIV). We chose the periodate-oxidation product (IV) of methyl 4 : 6-*O*-benzylidene-α-D-glucoside, and the product (V) of its partial acidic hydrolysis. α-Anomers were chosen for convenience of preparation and this configuration is not expected to influence comparison with periodate oxycellulose.

Additional acetal and hemiacetal cyclic systems which are possibly present in the material (IV) and almost certainly present in the product (V) are assumed not to have any marked influence on the alkaline degradation. The relative stability of the latter towards acidic hydrolysis suggests, however, possible formation of a six-membered ring,[7] and its slow reaction with sodium metaperiodate probably indicates ring closure between $C_{(2)}$ and $C_{(4)}$ to give the dioxan (VI), or possibly a fused-ring system resulting from further acetal formation by the remaining free aldehyde group.

The benzylidene derivative (IV), which carries a cyclic acetal substituent in the α-carbonyl position, was treated with lime-water at room temperature. Although only sparingly soluble in water, it dissolved much more readily in lime-water and was reprecipitated unchanged if the solution was immediately saturated with carbon dioxide (this may indicate salt or complex formation). After 30 min. at room temperature the lime-water solution yielded glycollic acid (IX) and 4-formyl-2-phenyl-2*H*, 6*H*-1 : 3-dioxin (VII) in approximately equal amounts, together with unchanged material (IV) and products arising from a Cannizzaro reaction. Identification of the dioxin derivative (VII) is based on its elemental analysis, the yield of benzaldehyde on acidic hydrolysis, and on the fact that after acidic hydrolysis and treatment with lime-water paper-chromatographic evidence of αγ-dihydroxybutyric acid (X) was obtained.

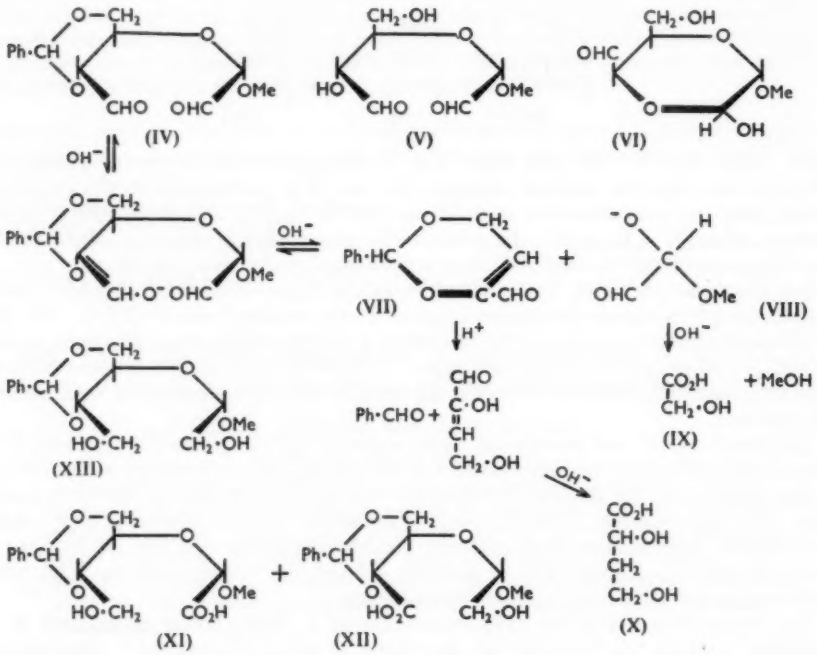
From this degradation we also isolated a mixture of the acids (XI) and (XII) (approx. ratio 3 : 1) arising from an intramolecular Cannizzaro reaction of the starting material (IV). This reaction apparently accounted for about 20% of the starting material decomposed for both short and long treatments. No neutral product (XIII) could be detected, so it was concluded that intermolecular Cannizzaro reactions were not important. The dioxin derivative (VII) decomposed slowly in lime-water at room temperature, liberating benzaldehyde and a complex mixture of acidic products, and depositing an insoluble resin; this degradation was evidently complex and was not investigated.

Degradation of dialdehyde (V) by lime-water at 25° resulted in the rapid formation of

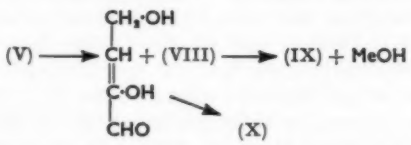
[7] Cf. Cadotte, Dutton, Goldstein, Lewis, Smith, and van Cleve, *J. Amer. Chem. Soc.*, 1957, **79**, 691; Richards, *J.*, 1957, 3222.

[8] Kenner and Richards, *J.*, 1956, 2921.

glycollic (IX) and αγ-dihydroxybutyric (X) acids, which were shown by quantitative paper chromatography to be present in approximately equivalent amount and to correspond to 72% degradation of the aldehyde (V) after 24 hr. Both acids were identified as crystalline derivatives. Volatile acids (10% of total acidity) produced simultaneously consisted mostly of formic acid, and unidentified neutral compounds were also formed



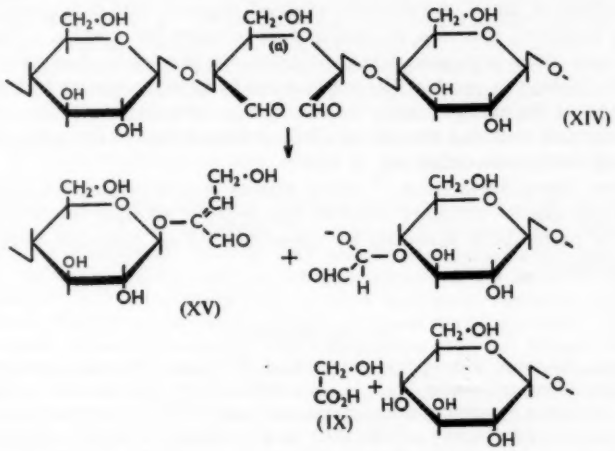

(*ca.* 15%, possibly including unchanged V) under these conditions. Further slow formation of small amounts of acid in the lime-water solution was not studied further. No conclusive evidence was obtained of a Cannizzaro reaction but qualitative paper chromatography suggested that it may occur to a very small extent.




Each of the products of the reactions described above is in accordance with the reaction mechanisms shown and it is therefore probable that the same type of alkaline degradation will apply also in periodate oxycellulose. This implies that the alkaline degradation of periodate oxycellulose, such as was observed by Davidson,[1] ultimately results from scission of the C–O bond (a) of the oxidised unit, as proposed by Haskins and Hogsed [4] and by Corbett and Kenner.[9] Thus in the case of an isolated oxidised unit the scission may be represented as illustrated.

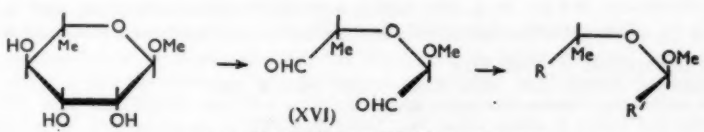
[9] Corbett and Kenner, *J.*, 1953, 2245.

Further, the equivalence of the yields of glycollic and αγ-dihydroxybutyric acids from alkaline degradation of the aldehyde (V) is very significant. Earlier experiments on the alkaline degradation of 3-*O*-methyl-D-glucose [10] indicated that the rearrangements which result in formation of D-gluco*meta*saccharinic acid, proceed almost quantitatively in lime-water at room temperature, and this system is analogous to the sequence of reactions




which result in formation of αγ-dihydroxybutyric acid (X) from the aldehyde (V). Hence the observation that glycollic and αγ-dihydroxybutyric acid were formed in equivalent amount by action of lime-water may be interpreted as an indication that the glyoxal derivative (VIII) undergoes complete degradation to glycollic acid (IX) as shown above. This was supported by identification of methanol. It follows that one molecule of glycollic acid should be liberated for each chain scission under these conditions.

The extent of subsequent alkaline rearrangement of an intermediate of type (XV) is however much less certain. Although Haskins and Hogsed [4] have suggested that an intermediate of this type will undergo simultaneous hydrolysis and hydration with formation of a tetrose, this seems unlikely. Thus for example, in the case of the benzylidene derivative (IV), where the glucosyl acetal linkage is replaced by a cyclic acetal grouping, the relevant intermediate (VII) was comparatively stable to lime-water, but underwent a slow and apparently complex degradation at room temperature, with liberation of benzaldehyde. The possibility of degradation of the intermediate (XV) from the oxycellulose is dependent on scission of the glycosyl linkage in (XV) and this will be further investigated.




It is probable that not every oxidised unit in periodate oxycellulose will undergo scission in alkali: Cannizzaro rearrangement may intervene, and would yield an acidic polysaccharide. The Cannizzaro rearrangement has previously been observed [11,2] with

[10] Kenner and Richards, *J.*, 1954, 278.
[11] Fry, Wilson, and Hudson, *J. Amer. Chem. Soc.*, 1942, **64**, 872.

periodate-oxidation products such as (XVI), which do not contain a β-alkoxycarbonyl grouping. The results were therefore not complicated by the simultaneous occurrence of the scission reaction and it is probable that some of the periodate-oxidation products whose alkaline degradation was studied by Head [3] also underwent the Cannizzaro rearrangement for similar reasons.

Cannizzaro rearrangements have previously been postulated [5] to explain the acids produced by action of alkali on periodate-oxidised starches, but it is probable that most of the acidity observed was due to simple acids arising by scission. The apparently greater importance of the intramolecular Cannizzaro reaction for the benzylidene derivative (IV) than for its hydrolysis product (V) may be due to steric factors or to a slower scission as a consequence of the alkali-stability of the dioxin intermediate (VII). Experimental difficulties involved in studying the rate of alkaline degradation of the compound (IV) have so far prevented further investigation of this.

The modified Barry degradation,[12] which utilises *cyclo*hexylamine instead of phenylhydrazine acetate, almost certainly involves the type of alkaline degradation indicated above, which is particularly favoured by separation of an insoluble derivative of the glyoxal intermediate.

## Experimental

The following solvents and sprays were used in paper chromatography. Solvent *a*, butan-1-ol–pyridine–benzene–water (4 : 2 : 1 : 1); solvent *b*,[13] ethyl acetate–acetic acid–water (10 : 1 : 3 : 1); solvent *c*,[14] ethyl acetate–acetic acid–water (3 : 1 : 1); solvent *d*, butan-1-ol–ethanol–water (4 : 1·1 : 1·9); spray *a*,[16] B.D.H. " 4·5 " indicator; spray *b*,[17] sodium periodate–permangate; spray *c*, 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid; spray *d*,[18] *p*-anisidine; spray *e*,[19] silver nitrate–sodium hydroxide; spray *f*,[20] hydroxylamine–ferric chloride.

*Acid Determinations.*—(a) *Total acids.* All acid yields were determined by back-titration after treatment at room temperature for 30 min. with a four-fold excess of 0·025N-sodium hydroxide, the final concentration of alkali being not less than 0·01N.

(b) *Volatile acids.* Volatile acids and the proportion of formic acid were determined as described earlier.[21]

(c) *Glycollic acid.* After separation by paper chromatography glycollic acid in aqueous solution was determined spectrophotometrically by Calkins's method.[22]

2 : 4-O-*Benzylidene*-3-O-(D-1-*methoxy*-2-*oxoethyl*)-D-*erythrose.*—This compound, m. p. 142—144°, was prepared by oxidation with sodium metaperiodate of methyl 4 : 6-*O*-benzylidene-α-D-glucoside.[23]

*Alkaline Degradation.*—(a) *Qualitative.* A suspension of the benzylidene derivative (12·0 g.) was stirred with oxygen-free 0·04N-calcium hydroxide (3950 ml.) at 20°. After *ca.* 1 hr. the smell of benzaldehyde became apparent and a brown resin separated.[24] After 16 hr. the mixture was filtered from resin and unchanged material (total wt. 3·92 g.), and excess of carbon dioxide was added to the filtrate which was then extracted with ether (3 × 500 ml.). The extracts were evaporated leaving, after removal of benzaldehyde by steam-distillation [2 : 4-dinitrophenylhydrazone (0·4 g.), m. p. 228—232°], a syrupy residue (0·40 g.), $R_F$ 0·88 in solvent *d* (sprays *b*, *c*, *e*). This product, 4-*formyl*-2-*phenyl*-2H,6H-1 : 3-*dioxin*, recrystallised from ether

[12] Barry and Mitchell, *J.*, 1953, 3610.
[13] Moilanen and Richtzenhain, *Acta. Chem. Scand.*, 1954, **8**, 704.
[14] Loffler and Reichl, *Mikrochim. Acta.*, 1953, 79.
[16] Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677.
[16] Nair and Muthe, *Naturwiss.*, 1956, **43**, 106.
[17] Lemieux and Bauer, *Analyt. Chem.*, 1954, **26**, 920.
[18] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[19] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[20] Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 5859.
[21] Richards and Sephton, *J.*, 1957, 4492.
[22] Calkins, *Analyt. Chem.*, 1943, **15**, 762.
[23] Rowen, Forziati, and Reeves, *J. Amer. Chem. Soc.*, 1951, **73**, 4484.
[24] Cf. Kenner and Richards, *J.*, 1955, 1709.

as needles, m. p. 70—71° (Found: C, 69·2; H, 5·4; Ph·CHO, 53·8. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·3; Ph·CHO, 55·6%). The product slowly decomposed at room temperature.

The aqueous residue after concentration to *ca.* 800 ml. was filtered from calcium carbonate and, after further concentration to 100 ml., the precipitated calcium glycollate tetrahydrate (3·66 g.) [Found: $H_2O$, 27·4. Calc. for $(C_2H_3O_3)_2Ca,4H_2O$: $H_2O$, 27·5%] was separated and characterised as its 4-bromophenacyl ester, m. p. and mixed m. p. 138—141°. Evaporation to dryness yielded a further quantity of calcium salts (3·90 g.) of which part (1·9 g.) dissolved in hot absolute alcohol (150 ml.). Treatment with Amberlite resin IRC-50 followed by paper chromatography revealed glycollic acid ($R_F$ 0·51, solvent *c*) and a component $R_F$ 0·82 (solvent *c*; sprays *a*, *c*, *d*). Treatment of this alcohol-soluble material with a mixture of Amberlite resins IR-120(H) and IR-4B(OH) removed the material completely from solution. Hydrolysis in 0·1N-hydrochloric acid at 60° for 1 hr. gave a mixture containing benzaldehyde, glyoxylic acid, glycollaldehyde, and erythritol, which were each identified as described below. A component corresponding to D-erythronolactone was disclosed by paper chromatography ($R_F$ 0·39; solvent *b*, sprays *e*, *f*).

(b) *Quantitative.* The finely powdered erythrose derivative (9·48 g., 30 mmole) was stirred with oxygen-free 0·041N-calcium hydroxide (2·5 l.) at room temperature. After 20 min. the material had almost completely dissolved and excess of carbon dioxide was added. The unchanged material (5·1 g., 16·1 mmoles) which then separated was removed and the filtrate concentrated to 900 ml. The precipitated calcium carbonate together with some more unchanged material (0·60 g.; 1·9 mmoles) was filtered off and the filtrate extracted continuously with ether for 24 hr. The ethereal extract was concentrated to 30 ml., filtered from unchanged material (0·12 g., 0·33 mmoles) and on evaporation to dryness yielded the crude dioxin (1·453 g., 7·65 mmole), m. p. 58—60° rising to 70—71° after one recrystallisation from ether.

An aliquot portion (5 ml.) of the ether-extracted aqueous solution (total vol. 875 ml.) was stirred with Amberlite resin IR-120(H) (2·0 ml.) for 10 min., then filtered and the total acids in the aqueous solution were determined (10·44 mequiv.). On evaporation of the remaining solution to dryness, calcium salts (1·537 g.) were obtained. The equivalent weight (147) derived from these results corresponds to a mixture of calcium glycollate tetrahydrate (81%) and Cannizzaro rearrangement products $(C_{14}H_{17}O_7)_2Ca$ (19%). Extraction of the mixture with hot absolute alcohol (200 ml.) yielded alcohol-soluble salts (0·42 g.), the benzaldehyde content (21·4%) of which corresponds to 64·1% of Cannizzaro rearrangement products in the alcohol-soluble fraction, or 17·5% in the total calcium salts. The products of acidic hydrolysis of the alcohol-soluble calcium salts were examined as follows:

(i) *Benzaldehyde.* A solution of the alcohol-soluble calcium salts (0·617 g.) in 0·1N-hydrochloric (100 ml.) was heated at 60—65° and the liberated benzaldehyde removed by a stream of nitrogen and collected in excess of 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid (2—3 hr. required). Benzaldehyde 2 : 4-dinitrophenylhydrazone separated at 0° (0·368 g., 1·29 mmoles; m. p. and mixed m. p. 239—241°).

(ii) *Glycollaldehyde and glyoxylic acid.* The hydrolysis mixture after removal of the benzaldehyde was made 2N with respect to hydrochloric acid and a solution (30 ml.) of 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid added. The mixture was heated for 2—3 hr. at 100° and kept at 0° overnight, and the precipitate (0·294 g.) was collected, washed with boiling alcohol, and identified as glyoxal bis-2 : 4-dinitrophenylhydrazone (0·103 g., 0·25 mmole), m. p. and mixed m. p. 323—325° (decomp.). Glyoxylic acid 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 193—195°, was isolated from the alcohol extract.

(iii) *Erythritol.* A further sample of the alcohol-soluble calcium salts (0·620 g.) was heated with 0·5N-sulphuric acid (100 ml.) at 100°, the benzaldehyde being removed by a stream of nitrogen. After 2 hr. the mixture was de-ionised by stirring with mixed Amberlite resins IRA-400(OH) and IR-120(H), and the solution on evaporation yielded erythritol (0·115 g., 0·96 mmole), m. p. and mixed m. p. 117—119°.

3-O-(D-1-*Methoxy*-2-*oxoethyl*)-D-*erythrose*.—2 : 4-*O*-Benzylidene-3-*O*-(D-1-methoxy-2-oxoethyl)-D-erythrose (31·6 g.) was suspended in 0·01N-sulphuric acid and heated, with stirring, at 70° for 1 hr. The mixture was cooled, unchanged material (0·3 g.) removed, and the aqueous layer extracted with ether to remove benzaldehyde. After neutralisation with Amberlite resin IR-4B(OH), the solution was evaporated to dryness, leaving a clear syrup (18·5 g.) which was shown by paper chromatography (solvent *a*, sprays *b* and *e*) to consist mainly of one component ($R_F$ 0·70), with traces of a second component ($R_F$ 0·39). When this mixture was

XUM

chromatographed on a carbon–Celite [15] column, erythrose was eluted by water (4 l.). Elution was then continued with 10% aqueous ethanol, and the desired erythrose derivative ($R_F$ 0·70) was obtained as a clear colourless syrup (13·0 g.), $[\alpha]_D^{22}$ +88·0° (*c* 3·183 in $H_2O$) (Found: C, 43·7; H, 5·19; OMe, 15·3. $C_7H_{12}O_6$ requires C, 43·7; H, 6·2; OMe, 16·1%).

*Reaction of* 3-O-(D-1-*Methoxy*-2-*oxoethyl*)-D-*erythrose with Phenylhydrazine.*—(a) *Acid conditions.* The dialdehyde (0·40 g.) in 15% acetic acid (20 ml.) was heated at 100° for 3 min. with phenylhydrazine (2·0 g.). The yellow precipitate was glyoxal phenylosazone, m. p. and mixed m. p. 167—168° (after one crystallisation from alcohol–water). The filtrate was heated for a further 40 min. at 100° and the solid obtained (0·2 g.) was identified as erythrose phenylosazone, m. p. 162—164° (Found: C, 63·7; H, 6·7. Calc. for $C_{16}H_{18}O_3N_4$: C, 64·4; H, 6·0%).

(b) *Neutral conditions.* (i) The dialdehyde (0·2 g.) and sodium acetate (0·9 g.) were dissolved in water (10 ml.), and phenylhydrazine hydrochloride (0·5 g.) was added. The mixture was kept at room temperature for 5 min.; the oil which separated readily recrystallised from alcohol and was glyoxal phenylosazone, m. p. and mixed m. p. 167—169°.

(ii) Shaking the dialdehyde (0·3 g.) with water (20 ml.) and phenylhydrazine hydrochloride (0·7 g.) at room temperature for 5 min. gave glyoxal osazone, m. p. and mixed m. p. 166—168°.

*Acid Hydrolysis of* 3-O-(D-1-*Methoxy*-2-*oxoethyl*)-D-*erythrose.* The dialdehyde (0·21 g.) in 0·1N-sulphuric acid (50 ml.) was heated in a boiling-water bath for 5 hr. The rotation fell to a constant value and paper chromatography indicated erythrose, the $R_F$ changing from 0·70 to 0·39 (solvent *a*; sprays, *b* and *e*). $[\alpha]_D^{20}$ +88° (initial); +35·2° (1 hr.); +2·5° (3 hr.); −1° (5 hr., const.).

*Periodate Oxidation of* 3-O-(D-1-*Methoxy*-2-*oxoethyl*)-D-*erythrose.*—The consumption of periodate by the dialdehyde (0·138 g.) in 0·004M-sodium metaperiodate (25 ml.), measured by reaction with acidic potassium iodide and titration with sodium thiosulphate, was 0·28 (10 min.), 0·42 (30 min.), 0·63 (2 hr.), 0·77 (5 hr.), 1·1 (24 hr.) mol.

*Alkaline Degradation of* 3-O-(D-1-*Methoxy*-2-*oxoethyl*)-D-*erythrose.*—(a) *Qualitative.* A solution of the dialdehyde (5·3 g.) in oxygen-free water (500 ml.) containing calcium hydroxide (2·5 g.) was kept at room temperature for 24 hr., then saturated with carbon dioxide and concentrated to *ca.* 100 ml. The distillate contained methanol but gave no reaction with 2 : 4-dinitrophenylhydrazine. The residual solution was filtered and the filtrate concentrated to a syrup (10—15 ml.), from which the calcium salts were precipitated by pouring the whole into alcohol–acetone (1 : 1; 200 ml.). The calcium salts were separated by filtration and extracted with dry methanol for 12 hr. in a Soxhlet extractor. The methanol extract was added to the alcohol–acetone solution, and the mixture was evaporated to dryness, yielding a syrup (0·7 g.) which was shown by paper chromatography (solvent *a*) to consist mainly of approximately equal amounts of unchanged material ($R_F$ 0·70) and of an unidentified product ($R_F$ 0·52; solvent *a*, sprays *b* and *e*; $R_L$ 0·83, solvent *b*; L = lactic acid). Heating the neutral material with excess of sodium hydroxide removed the material of $R_L$ 0·83 (solvent *b*), and some αγ-dihydroxybutyric and glycollic acid were formed.

Paper-chromatographic examination (solvent *b*) of the free acids derived from treatment with Amberlite resin IR-120(H) of the calcium salts after methanol-extraction showed five components, *viz.*, glycollic acid ($R_L$ 0·80; sprays *a* and *b*), αγ-dihydroxybutyric acid ($R_L$ 0·64; sprays *a* and *b*), and its lactone ($R_L$ 1·00; sprays *b* and *f*), together with some neutral materials ($R_L$ 0·83 in solvent *b*; $R_F$ 0·52 and 0·70 in solvent *a*) and traces of a product ($R_L$ 0·51) which reacted with spray *c*. After separation on thick paper, the glycollic acid was characterised as its 4-bromophenacyl ester, m. p. and mixed m. p. 138—140°, and αγ-dihydroxybutyric acid as its brucine salt, 169—171° (Found: N, 5·45. Calc. for $C_{27}H_{34}O_8N_2$: N, 5·45%). The same brucine salt was also obtained by fractional crystallisation of the mixed brucine salts from alcohol–ether.

Because of the difficulty of removing all the neutral material further examination of the acids was carried out after purification by means of ion-exchange resins as described for the quantitative experiments below. After purification in this way, paper chromatography showed the presence of all the compounds noted above except the neutral material ($R_L$ 0·83). After the acid solution had been heated with Amberlite resin IR-120(H) for 1 hr. at 60°, the material of $R_L$ 0·51 (solvent *b*) disappeared and a trace of a component corresponding to erythronolactone (solvent *a*; spray *f*) was detected.

(b) *Quantitative.* Oxygen-free nitrogen was passed through an aqueous solution (10 ml.) of the dialdehyde (0·1489 g.) and oxygen-free 0·0446N-calcium hydroxide (90 ml.) was added.

Samples (5·0 ml.) were withdrawn periodically and the alkali consumption determined in the usual way.[25]

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Acids produced (equiv.) ..... | 0·14 | 0·65 | 0·96 | 1·23 | 1·37 | 1·47 | 1·56 | 1·63 |
| Time (hr.) ..... | 0·05 | 0·33 | 1·0 | 3·5 | 24 | 72 | 168 | 384 |

In a separate experiment the dialdehyde (1·5247 g.) was dissolved in oxygen-free 0·04N-lime-water (1500 ml.). After 24 hr. the acids formed (12·45) were determined by treatment of an aliquot portion with Amberlite IR-120(H) resin (2·0 ml.), and the reaction was stopped by addition of excess of carbon dioxide. The mixture was concentrated to 500 ml., filtered from calcium carbonate, and the filtrate further concentrated to *ca.* 250 ml. A portion of the distillate (500 ml.) gave a very slight precipitate (5—10 mg.) with 2 : 4-dinitrophenylhydrazine reagent and gave no reaction with acidified Schiff's reagent.[26]

The aqueous reaction mixture was treated with Amberlite resin IR-120(H) (30 ml.) for 20—30 min. The resin was then removed by filtration and washed free from acid, and the combined filtrate and washings were stirred overnight with Amberlite resin IRA-400 (40 ml., carbonate form).[27] The resin, after transfer to a column containing a further 5 ml. of the same resin, was washed free from neutral products with distilled water (4 l.). Evaporation of the washings yielded a thick syrup (0·227 g.), which paper chromatography showed to consist of a number of products. The adsorbed acids were eluted from the resin with N-ammonium carbonate (2 l.). The solution of ammonium salts and excess of ammonium carbonate was concentrated to *ca.* 100 ml., heated at 65—70° for 1½—2 hr. to destroy any residual carbonate, and then diluted to 250 ml. This stock solution was then examined as follows.

The solution of ammonium salts (100 ml.) was stirred with Amberlite resin IR-120(H) (10 ml.) for 1 hr. The resin was separated by filtration and washed and the filtrate and washings were diluted to 250 ml. to give a standard solution of the free acids. Aliquot portions of this solution were used to determine the yields of total acids (12·25 mequiv.), volatile acids (1·22 mequiv.), and formic acid (0·98 mequiv.).

A further sample (100—150 ml.) of the solution of ammonium salts was concentrated to *ca.* 10 ml. and then shaken with Amberlite resin IR-120(H) (6 ml.) for 1 hr. The resin was separated by filtration and washed with a small amount of water. The strength of the acid solution (*ca.* 12 ml.) was determined and a suitable quantity (1·5—2 mequiv.) applied to Whatman No. 3 MM paper (22 in. × 24 in.), which was irrigated for 6—7 hr. with solvent *b*. The paper was dried for 40 hr. in a current of air at room temperature, and guide strips were cut off and developed in the usual way with spray *a* and, on the reverse side of the strip, spray *f*. The appropriate sections of the paper were then eluted with water, and the acids and lactones present determined by back-titration, the yield of glycollic acid being confirmed by Calkins's method.[22] In two determinations the ratio of αγ-dihydroxybutyric acid (including lactone) to glycollic acid was 1·02 and 1·11. The total recovery, after allowance for guide strips and volatile acids, was 81%.

This work forms part of a programme of fundamental research undertaken by the Council of the British Rayon Research Association.

British Rayon Research Association,
Heald Green Laboratories,
Wythenshawe, Manchester, 22.

[*Received, October 21st*, 1957.]

[25] Kenner and Richards, *J.*, 1954, 1784.
[26] Hoffpauir and Reeves, *Analyt. Chem.*, 1949, **21**, 815.
[27] Cf. Machell, *J.*, 1957, 3389.

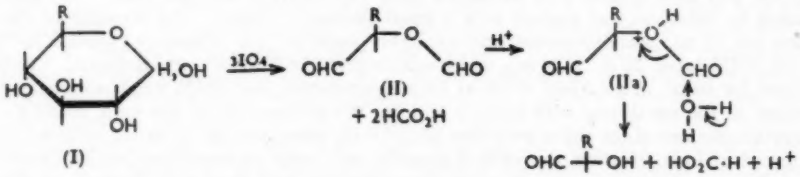
XUM

## 239. *The Oxidation of Monosaccharides by Periodate with Reference to the Formation of Intermediary Esters.*

By L. Hough, T. J. Taylor, G. H. S. Thomas, and B. M. Woods.

A study of the reactions of various monosaccharides with sodium metaperiodate at pH 3·6 at room temperature and in the dark has provided further evidence that the sugars are oxidised in their cyclic forms with the formation of intermediary esters. The different rates of hydrolysis of these esters have been related to the inductive effects of electrophilic groups in the alcohol component ($CO_2H$ > CHO > $CH_2$·OH > Me, H). The behaviour of various related compounds possibly arising during the oxidation of carbohydrates has been examined.

Various *O*-substituted aldohexoses are oxidised by periodate in their pyranose forms to give formyl esters which are sensitive to pH. Alkaline or strongly acid conditions cause rapid hydrolysis of these esters, but they are relatively stable in weak acid (pH 3—5).[1] Thus, at about pH 4 the consumption of oxidant by many reducing disaccharides, methylated aldoses, and aldose phosphates is considerably reduced owing to the intervention of formyl esters. This knowledge had made possible the preparation, *via* formyl esters, of 2-deoxy-D-ribose from 3-deoxy-D-glucose,[2] of 4-*O*-formyl-2-*O*-methylsulphonyl-D-arabinose from 3-*O*-methylsulphonyl-D-glucose,[3] of D-glyceraldehyde 3-phosphate from D-glucose 6-phosphate,[4] and of various *O*-methylaldopentoses from *O*-methylaldohexoses.[5] However, there is little information concerning the mode of oxidation of unsubstituted monosaccharides and few quantitative studies have been carried out. Schöpf and Wild [6] treated D-glucose (I; R = $CH_2$·OH) with sodium metaperiodate (3 mol.) and obtained formic acid (2 mol.) and α-*O*-formyl-D-glyceraldehyde (II; R = $CH_2$·OH; 1 mol.), providing



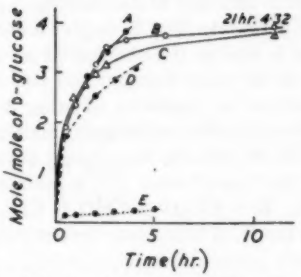

evidence that D-glucose is oxidised almost entirely, if not all, in the pyranose form. This conclusion is substantiated by Hughes and Nevell's observations [7] who noted that the theoretical 5 mol. of oxidant were rapidly reduced in neutral solution, whereas at pH 4·6, 3 mol. reacted rapidly and then 2 mol. much more slowly. Significantly determinations [8] of formaldehyde formed on oxidation of monosaccharides and, in particular, their *O*-methyl derivatives are invariably less than 1 mol. when carried out at below pH 7, as would be expected if the sugars were oxidised in their pyranose forms.

Oxidations have been followed by adding various crystalline monosaccharides to buffered (pH 3·6) periodate solution and, at intervals, determining the consumption of periodate and the formation of formaldehyde; the release of formic acid was also studied,

[1] Neumüller and Vasseur, *Arkiv Kemi*, 1953, **5**, 235.
[2] Gorin and Jones, *Nature*, 1953, **172**, 1057.
[3] Smith, D. C. C., *Chem. and Ind.*, 1955, 92; *J.*, 1957, 2690.
[4] Morrison, Rouser, and Stotz, *J. Amer. Chem. Soc.*, 1955, **77**, 5156.
[5] Barker and Smith, D.C.C., *Chem. and Ind.*, 1952, **30**, 1035; Hemming and Ollis, *ibid.*, 1953, 85; Fried and Walz, *J. Amer. Chem. Soc.*, 1952, **74**, 5468; Huffman, Lewis, Smith, F., and Spriestersbach, *ibid.*, 1955, **77**, 4346.
[6] Schöpf and Wild, *Chem. Ber.*, 1954, **87**, 1571.
[7] Hughes and Nevell, *Trans. Faraday Soc.*, 1948, **44**, 941.
[8] Reeves, *J. Amer. Chem. Soc.*, 1941, **63**, 1476; Bell, *J.*, 1948, 992; Bell and Greville, *J.*, 1950, 1902; Greville and Northcote, *J.*, 1952, 1945.

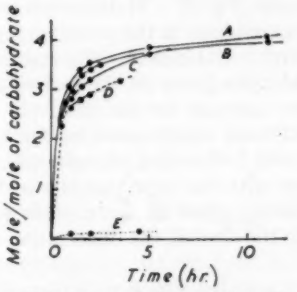
but in unbuffered solution (pH 2—4). Anomalies can arise in the determination of periodate uptake if during the estimation the reaction solution is made alkaline as in the Fleury–Lange method [9] or strongly acid as in the acid–thiosulphate method,[7] when rapid hydrolysis of the formyl ester will occur. For this reason, Neumuller and Vasseur's method,[1] whereby periodate is determined at pH 6·98, was selected and proved satisfactory. Similar errors can arise in estimates of formaldehyde, but were obviated by using the

FIG. 1.



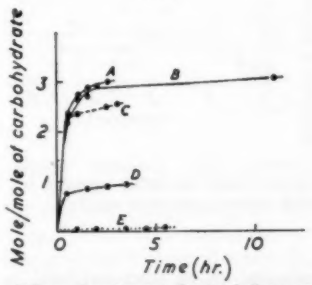

*A, β-D-Glucose, periodate uptake. B, αβ-D-Glucose (mutarotated), periodate uptake. C, α-D-Glucose, periodate uptake. D, α-D-Glucose, formic acid released. E, α-D-Glucose, formaldehyde released.*

FIG. 2.



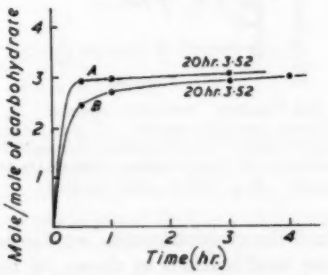

*A, α-D-Galactose, periodate uptake. B, αβ-D-Galactose (mutarotated), periodate uptake. C, β-D-Mannose, periodate uptake. D, α-D-Galactose, formic acid released. E, α-D-Galactose and β-D-mannose, formaldehyde released.*

FIG. 3.




*A, D-Ribose (mutarotated), periodate uptake. B, D-Ribose, α-D-xylose and β-L-arabinose, periodate uptake. C, D-Ribose, formic acid released. D, 3-O-Methyl-D-glucose, periodate uptake. E, D-Ribose, formaldehyde released.*

FIG. 4.




*A, α-L-Fucose, periodate uptake. B, α-L-Rhamnose, periodate uptake.*

chromotropic acid method [10] after complete removal of excess of periodate from the reaction mixture by precipitation with lead dithionate at pH 3·6.

The results (Fig. 1) obtained for α-D-glucose (I; R = $CH_2$·OH) are consistent with oxidation of the majority in the pyranose form with the rapid consumption of 3 mol. of periodate and the formation of D-glyceraldehyde formate (II; R = $CH_2$·OH). The rapid release of *ca.* 0·15 mol. of formaldehyde suggests that some 15% of the aldohexose was oxidised in either the furanose or the *aldehydo*-form. Oxidations of β-D-glucose and of αβ-D-glucose (a solution of α-D-glucose which had been allowed to mutarotate to equilibrium), although showing evidence of formyl ester intermediates, revealed differences

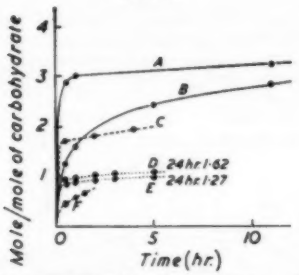
[9] Fleury and Lange, *J. Pharm. Chim.*, 1933, **17**, 196.
[10] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.

in the initial rapid reactions (Fig. 1), confirming the view that more than one form of the monosaccharide was concerned in the reaction.

α-D-Galactose and β-D-mannose gave similar results (Fig. 2) to those for D-glucose and the rapid release of formaldehyde (0·06—0·07 mol.) again indicated that a small amount was not oxidised in the pyranose form.

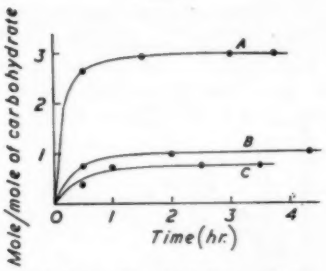
Oxidation in the pyranose form and subsequent formyl ester formation was even more apparent in the case of the aldopentoses since α-D-xylose (I; R = H), D-ribose, and β-L-arabinose showed very little reaction after the initial rapid consumption of 3 mol. of periodate (Fig. 3). Stabilisation was also apparent in the case of 3-*O*-methyl-D-glucose, which was oxidised in the pyranose form by 1 mol. of periodate (Fig. 3) to give 4-*O*-formyl-2-*O*-methyl-D-arabinose.[5] The stability of this ester is due to the absence of an electrophilic aldehyde group on the carbon atom adjacent to the ester linkage, and this explanation also accounts for the relatively stable esters formed on oxidation of other 3-*O*- and 4-*O*-substituted aldohexoses, as for example, the disaccharides, cellobiose, maltose, and lactose, and 1 : 3-linked oligoglucosaccharides.[1,11] These and the subsequent results are consistent with the view that the acid hydrolysis of the formyl ester (II) is influenced by the inductive effect of electrophilic substituents (II; R = $CO_2H$ > CHO > $CH_2$·OH > Me, H) in the alcohol, the dissociation of the oxonium ion (IIa) being rate-determining.

FIG. 5.




*A, β-D-Fructose, periodate uptake. B, L-Sorbose, periodate uptake. C, β-D-Fructose, acid released. D, L-Sorbose, formaldehyde released. E, β-D-Fructose, formaldehyde released. F, L-Sorbose, acid released.*

FIG. 6.




*A, Tartaric acid, periodate uptake. B, Glyoxylic acid, periodate uptake. C, Dimethyl tartrate, periodate uptake.*

The 6-deoxyaldohexoses, α-L-fucose and α-L-rhamnose, were also oxidised in their pyranose modifications as shown by the rapid consumption of 3 mol. of oxidant, further reaction being very slow (Fig. 4). The greater stability of the formyl esters of lactaldehyde (II; R = Me) and of glycollaldehyde (II; R = H) than of α-*O*-formylglyceraldehyde (II; R = $CH_2$·OH) must therefore be attributed to the absence of a neighbouring hydroxyl group.

Oxidations of hexuloses are more complex since they could theoretically be oxidised in the acyclic, furanose, or pyranose form by two possible routes in each case. Arni and Percival,[12] and Khouvine and Arragon,[13] have interpreted their results in terms of the acyclic forms, but, in agreement with Sprinson and Chargaff [14] our results at pH 3·6 favour oxidation in a cyclic form with the formation of ester intermediates (*e.g.*, III, V, VI, VIII). In the initial rapid reaction, β-D-fructose (IV) consumed 3 mol. of periodate with the formation of 1 mol. of formaldehyde and 1·5 equivalents of acid (Fig. 5) which, considered

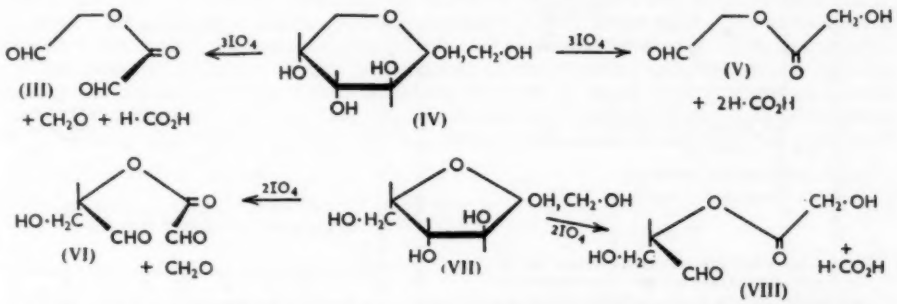
[11] Meyer and Rathgeb, *Helv. Chim. Acta*, 1948, **31**, 1540, 1545; Morrison, Kuyper, and Orten, *J. Amer. Chem. Soc.*, 1953, **75**, 1502; Head and Hughes, *J.*, 1954, 603; Manners and Archibald, *J.*, 1957, 2206.

[12] Arni and Percival, *J.*, 1951, 1822.

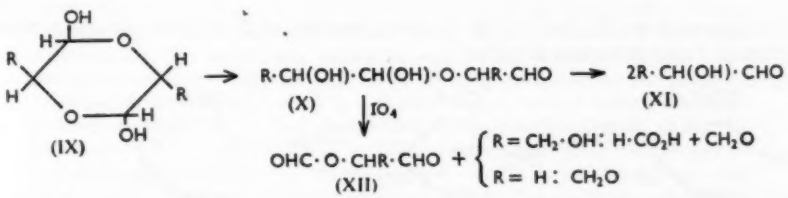
[13] Khouvine and Arragon, *Bull. Soc. chim. France*, 1941, **8**, 676.

[14] Sprinson and Chargaff, *J. Biol. Chem.*, 1946, **164**, 433.

with the slow over-oxidation typified by reaction of aldopentoses, suggests that the predominant pathway involves oxidation in the pyranose form with the formation of a glyoxylic ester (III) of glycollaldehyde. On the other hand, L-sorbose (VII) gave quite different results (Fig. 5) compatible with oxidation in the furanose form with the rapid formation of 1 mol. of formaldehyde and α-*O*-glyoxylylglyceraldehyde (VI). By comparison




with the oxidations of aldohexoses, this ester would be susceptible to hydrolysis and further oxidation. When dimethyl tartrate was oxidised with periodate at pH 3·6 only 1 mol. of oxidant reacted, confirming the view that glyoxylic esters can be stabilised at this pH; under the same conditions glyoxylic acid and tartaric acid consumed 1 and 3 mol. of oxidant respectively (Fig. 6).




Also of interest were the oxidations of DL-glyceraldehyde and glycollaldehyde which exist in their crystalline states as cyclic dimers (IX; R = $CH_2$·OH and H respectively).[15] The results (Fig. 7) show that unless they are left in solution for some time to revert to monomers (XI), they give rise to formyl esters (XII) as a result of oxidation of their acyclic dimers (X) which are presumably formed as intermediates between the monomeric (XI) and the cyclic dimeric state (IX).

At pH 3·6, methyl (methyl α-D-galactopyranosid)uronate (XIII; R = Me) consumed 3 mol. of periodate after 10 hr. and a further mol. after 50 hr. (Fig. 8), these resembling the results obtained at pH 4·5 by Edington, Hirst, and Percival;[16] this is compatible with previous suggestions[14] that the oxidation is arrested by the oxalyl ester (XVI; R = Me). This ester (XVI; R = Me) arises from the methyl ester methyl glycoside (XIII) by normal oxidative cleavage to the dialdehyde (XIV) followed by oxidation of the activated hydrogen atom[14,17] to the hydroxy-dialdehyde (XV) and subsequent oxidative cleavage. Such a mechanism was not operative in the case of sodium D-glucuronate at pH 3·6 since it reacted with 3 mol. of periodate in 0·5 hr., then with an extra 2 mol. in 6 hr. during which 1 mol. of carbon dioxide was liberated (Fig. 8); under these conditions oxalic acid was stable to periodate. Similar results were obtained by Sprinson

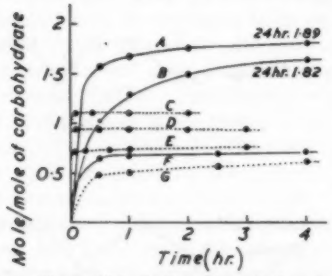
[15] Bergman and Miekeley, *Ber.*, 1929, **62**, 2297; 1931, **64**, 802; Summerbell and Rochen, *J. Amer. Chem. Soc.*, 1941, **63**, 3241; Baer and Fischer, *J. Biol. Chem.*, 1943, **150**, 213; Wohl and Neuberg, *Ber.*, 1900, **33**, 3095.

[16] Edington, Hirst, and Percival, *J.*, 1955, 2281.

[17] Huebner, Ames, and Bubl, *J. Amer. Chem. Soc.*, 1946, **68**, 1621.

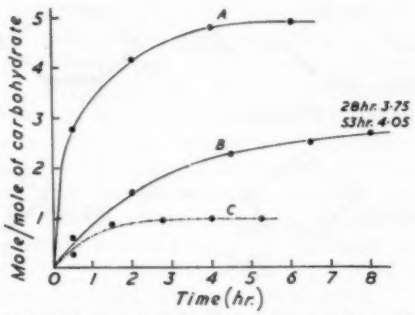
and Chargaff.[14] These observations can be accommodated by reaction of D-gluco-pyranuronic acid with 3 mol. of oxidant to give a formyl ester of tartronaldehydic acid (XVII), the hydrolysis of which would be facilitated by the carboxyl group next to the

FIG. 7.



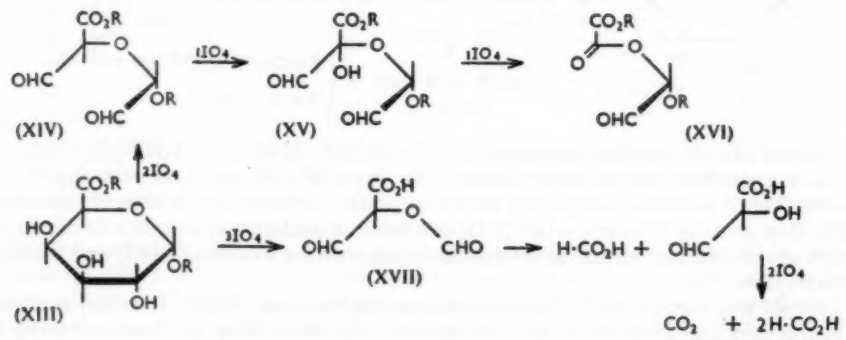

*A*, DL-*Glyceraldehyde* (*kept in solution for* 15 *hr.*), *periodate uptake*. *B*, DL-*Glyceraldehyde*, *periodate uptake*. *C*, DL-*Glyceraldehyde*, *formaldehyde released on oxidation at* pH 7·5 (*bicarbonate buffer*). *D*, *Glycollaldehyde* (*kept in solution for* 24 *hr.*), *formaldehyde released*. *E*, *Glycollaldehyde*, *formaldehyde released*. *F*, *Glycollaldehyde*, *periodate uptake*. *G*, DL-*Glyceraldehyde*, *formaldehyde released*.

FIG. 8.




*A*, *Sodium* D-*glucuronate*, *periodate uptake*. *B*, *Methyl* (*methyl* α-D-*galactopyranosid*)*uronate*, *periodate uptake*. *C*, *Sodium* D-*glucuronate*, *carbon dioxide released*.

ester linkage and would lead to the further reaction of 2 mol. of periodate with the formation of 1 mol. of carbon dioxide.




## EXPERIMENTAL

The crystalline monosaccharides were dried at 60° under reduced pressure for 2 hr. Unless stated otherwise, the monosaccharide (*ca.* 30 mg., accurately weighed) was washed into a mixture of sodium acetate buffer solution (pH 3·6; 25 ml.) and sodium metaperiodate solution (0·3M; 5 ml.) and then made up to 100 ml. with water. The mixture was then quickly transferred to an amber bottle and kept in the dark at room temperature (*ca.* 18°).

The periodate uptake was determined on serial samples (10 ml.) by Neumüller and Vasseur's method,[1] the sample being pipetted into a *mixture* of phosphate buffer (pH 6·98; 25 ml.) and 20% potassium iodide solution (5 ml.) and the liberated iodine titrated with 0·01N-sodium thiosulphate solution (starch).[18]

[18] In collaboration with Mr. A. O. Pittet we have confirmed the results for D-glucose (Fig. 1) by using the ultraviolet spectrophotometric method (Aspinall and Ferrier, *Chem. and Ind.*, 1957, 1219) for the estimation of periodate at pH 3·6.

Formic acid was determined on serial samples (10 ml.) from a reaction mixture similar to that described above except that the acetate buffer was omitted. Ethylene glycol (2 ml.) was added to the sample and after *ca.* 15 min. the solution was titrated potentiometrically with 0·01N-sodium hydroxide; pH 6·25 was taken as the end-point.[19]

Formaldehyde was determined by O'Dea and Gibbons's method.[10] Samples (1 ml.) were withdrawn from a buffered solution and after the removal of excess of periodate with 20% w/v lead dithionate solution (1 ml.) the clear solution (1 ml.) was treated with the chromotropic acid reagent. The absorption was read on a colorimeter (E.E.L. Filter 626). The formaldehyde liberated from known amounts of erythritol was used for the preparation of the standard curve.

The evolution of carbon dioxide was followed in the Warburg apparatus in the dark by adding the carbohydrate (*ca.* 1 mg., accurately weighed) in water (1 ml.) to sodium acetate buffer (pH 3·6; 3 ml.) and allowing the manometer to equilibrate to the bath-temperature (18°) before closing the tap and tipping 0·3M-sodium metaperiodate (1 ml.) from the side-arm.[20]

THE UNIVERSITY, BRISTOL. [*Received, October 29th*, 1957.]

[19] Anderson, Greenwood, and Hirst, *J.*, 1955, 225.
[20] Hough and Woods, *Chem. and Ind.*, 1957, 1421.

---

## 240. *Vibrational Frequency Correlations in Heterocyclic Molecules. Part IV.*[1] *Indoxyl Derivatives.*

By S. J. HOLT, A. E. KELLIE, D. G. O'SULLIVAN, and P. W. SADLER.

Infrared spectra of *N*-methylindoxyl, thioindoxyl, and a series of substituted *N*-acetylindoxyls indicate that they all possess fully ketonic structures in the solid, in chloroform, and in carbon disulphide. Consequently, hydrogen bonding is absent from these compounds, but weak hydrogen-bonded association occurs in substituted *O*-acetylindoxyls. The method involving study of the effect of ring substituents on carbonyl frequencies, and utilization of σ–ν correlations to assign bands, has been applied to series of *N*- and *O*-acetylindoxyls, diacetylindoxyls, *N*-acetyloxindoles, and *N*-acetylisatins. Double σ–ν correlation exists with *N*-acetylindoxyls. Diacetylindoxyls provide good single correlation, but the substituent effects on the ester carbonyl frequencies in these compounds and in *O*-acetylindoxyls, after transmission through an indole ring and an oxygen atom, are not linearly related to σ values. These correlations indicate frequency assignments. No evidence of σ-correlations was observed with *N*-acetylisatins, but comparison with isatins permits tentative band assignments for these compounds and for *N*-acetyloxindoles. The infrared results conclusively confirm the accepted formulæ for the *N*- and *O*-acetylindoxyls.

IN previous Parts [1-3] investigations were made of carbonyl frequencies of certain bicyclic compounds in which the second ring possessed negligible aromatic character. Substituent effects were those of substituted benzenes. Here attention is devoted to indoxyl derivatives and, although many of the compounds studied are effectively substituted benzenes, *O*-acetylindoxyls possessing the indole ring-system probably exhibit more complex substituent effects. Unfortunately, it has not been possible to determine the infrared spectra of indoxyls themselves, and consequently no further light has been shed on their tautomeric structures and ease of oxidation to corresponding indigos. Apart from the investigation of tautomeric and hydrogen-bonded structures, substituent effects, and band assignment, infrared study of *N*- and *O*-acetylindoxyls was desirable to confirm the usually accepted structures of these two sets of compounds. This verification is of some importance in

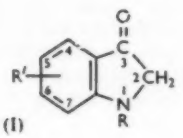
[1] Part III, O'Sullivan and Sadler, *J.*, 1957, 2916.
[2] *Idem*, *J.*, 1956, 2202.
[3] Kellie, O'Sullivan, and Sadler, *J.*, 1956, 3809.

view of the use of the *O*-acetyl derivatives as stain-producing substrates for the cytochemical localization of esterases in tissues and cells.[4]

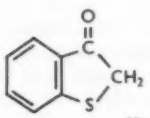
## Results and Discussion

(a) *Structures and Hydrogen Bonding.*—1-Methylindoxyl (I; R = Me, R′ = H), 1-acetylindoxyl (I; R = Ac, R′ = H), and thioindoxyl (II) might possess enolic structures, but the complete absence of absorption in the 3 μ region in the solid in chloroform and in carbon disulphide indicates that the compounds exist in the fully ketonic form. Indeed, no strong absorption occurs at greater frequencies than the intense carbonyl stretching maxima near 1750 cm.$^{-1}$; even the CH stretching frequency is of very low intensity. This not only confirms the ketonic structures but, taken in conjunction with the existence of NH absorption in indoxyl acetates, proves conclusively that the *N*- and *O*-acetylindoxyls have been assigned the correct structures. Substituents (F, Cl, Br, I, Me, MeO) in the 1-acetylindoxyl molecule (I; R = Ac) do not radically alter its absorption pattern, confirming the ketonic structure of these compounds previously indicated by such chemical behaviour as ready formation of oximes and semicarbazones. As the 1-acetyl compounds and thioindoxyl exist in their keto-forms, hydrogen bonding cannot occur, but their relatively high melting points indicate high lattice energies arising possibly from dipolar association. However, substituted indoxyl acetates (III; R = H, R′ = H, F, Cl, Br, I, Me, MeO, $CF_3$; R″ = Ac) possess intermolecular CO · · · HN links, producing broad bands with maxima between 3340 and 3270 cm.$^{-1}$.

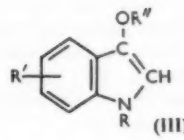
(b) *Band Assignments for Indoxyl Acetates.*—The NH stretching frequencies between 3340 and 3270 cm.$^{-1}$ are typical of heterocyclic imines participating in weak CO · · · HN bonding,[2,3,5] but the additional sharp peaks near 3450 cm.$^{-1}$ in oxindoles [3] and isatins [2] are absent. 1-Methylindoxyl acetate and 1-acetylindoxyl naturally show no NH absorption, and overtones [6] which sometimes exist are absent from this region. The carbonyl stretching frequencies are near 1740 cm.$^{-1}$. Absorption at about 1620 cm.$^{-1}$ is produced by CC stretching vibrations of the benzene ring.[7] In the 4- and 6-substituted compounds this band has half the carbonyl intensity but it is weak in other derivatives. The band just below 1500 cm.$^{-1}$ is also a benzene ring vibration,[8] and that near 1560 cm.$^{-1}$, absent from the 1-methyl and 1-acetyl compounds, is the NH deformation mode.



(I)



(II)



(III)

Probable assignments for the remaining bands in Table 1 are as follows: 1440 and 1370 cm.$^{-1}$ regions (methyl bending modes), strong band near 1340 cm.$^{-1}$ (Ph–N stretching vibration), intense absorption near 1220 cm.$^{-1}$ (C–O–C stretching frequency) [9] accompanied by slightly less intense maxima near 1080 and 910 cm.$^{-1}$ (other ester vibrations), strong absorption in the 820—780 cm.$^{-1}$ segment (out-of-plane bending motions in 1 : 2 : 3- or 1 : 2 : 4-trisubstituted aromatic ring).[10] The acetate band of 7-trifluoromethylindoxyl

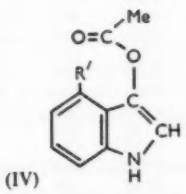
[4] Holt, *J. Histochem. Cytochem.*, 1956, **4**, 548.
[5] Sutherland, *Discuss. Faraday Soc.*, 1950, **9**, 274; Richards and Thompson, *J.*, 1947, 1248; Witkop, *J. Amer. Chem. Soc.*, 1950, **72**, 614; Witkop and Patrick, *ibid.*, 1951, **73**, 1558; Darmon and Sutherland, *Nature*, 1949, **164**, 440.
[6] Letaur and Gropp, *J. Chem. Phys.*, 1953, **21**, 1621.
[7] Colthup, *J. Opt. Soc. Amer.*, 1950, **40**, 397.
[8] Bornstein, *Analyt. Chem.*, 1953, **25**, 512.
[9] Thompson and Torkington, *J.*, 1945, 640.
[10] McCauley, Lien, and Launer, *J. Amer. Chem. Soc.*, 1954, **76**, 2354.

acetate is complicated by the CF stretching frequencies which fall in this region and probably give rise to the 1260 and 1240 cm.$^{-1}$ maxima.

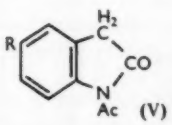
TABLE 1. *Frequencies of indoxyl acetates in potassium bromide discs.*

| Subst. | Frequencies (cm.$^{-1}$) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 4-Cl | 781 | 908 | 1048 | 1220 | 1330 | 1373 | 1435 | 1496 | 1577 | 1618 | 1741 | 3290 |
| 5-Cl | 804 | 896 | 1093 | 1220 | 1344 | 1373 | 1436 | 1473 | 1550 | 1618 | 1740 | 3330 |
| 6-Cl | 804 | 910 | 1078 | 1220 | 1336 | 1370 | 1456 | 1483 | 1580 | 1620 | 1742 | 3270 |
| 7-Cl | 785 | 915 | 1095 | 1226 | 1344 | 1373 | 1446 | 1500 | 1550 | 1620 | 1735 | 3280 |
| 5-Me | 800 | 911 | 1097 | 1223 | 1347 | 1371 | 1430 | 1495 | 1550 | 1617 | 1739 | 3340 |
| 5-Br | 800 | 910 | 1083 | 1227 | 1340 | 1374 | 1428 | 1465 | 1548 | 1620 | 1740 | 3300 |
| 7-$CF_3$ | 802 | 928 | 1096 | 1200<br>1240<br>1260 | 1321 | 1370 | 1438 | 1467 | 1555 | 1620 | 1730 | 3320 |
| 4-Cl, 5-Br | 796 | 910 | 1095 | 1223 | 1331 | 1367 | 1430 | 1460 | 1566 | 1603 | 1740 | 3280 |
| None | 814 | 910 | 1072 | 1225 | 1351 | 1372 | 1431 | 1462<br>1493 | 1550 | 1620 | 1743 | 3320 |
| 1-Me | 801 | 900 | 1026 | 1230 | 1343 | 1375 | 1434 | 1477 | — | 1614 | 1733 | — |
| Compd. | | | | | | | | | | | | |
| *N*-Acetylindoxyl | 764 | — | — | — | 1357 | 1388 | 1421 | 1466 | — | 1607 | 1674<br>1716 | — |

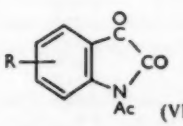
(c) *Carbonyl Stretching Frequencies of Indoxyl Acetates.*—Usual solvent effects are discernible in Table 2, the carbonyl frequencies being highest in carbon disulphide, significantly lower in the more polar chloroform, and, in general, slightly lower in the solid state, but here the shifts are more erratic. The effect of substituents is complex but frequency shifts are small and show a very rough tendency to increase with the Hammett $\sigma$ values [11] of substituents in view of their location with reference to position 3 ($\sigma_{Ph\text{-}O}$). A linear relation between carbonyl frequencies and $\sigma$ values is not to be expected as this system is not a simple substituted benzene, the substituent effects being transmitted first through the indole ring system and then through an oxygen atom. There is little consistency in the individual substituent effects in the two solvents (Table 2) and only very rough correspondence with substituent effects on the corresponding carbonyl frequencies in diacetylindoxyls (Table 3). Substitution at the imino-group has little influence on the carbonyl frequency (1-methyl-, 1-benzyl-, 1-carboxymethyl-, and the unsubstituted compound possessing maxima in chloroform at 1737, 1738, 1736, and 1738 cm.$^{-1}$ respectively), but extension of the ester side-chain appears to raise the frequency slightly (the acetate, propionate, and butyrate showing maxima in chloroform at 1738, 1744, and 1745 cm.$^{-1}$ respectively).



(IV)



(V)



(VI)

Usually, as the carbonyl stretching frequency of an acetate increases, the C–O–C frequency diminishes. Table 2 shows that this is not a general feature of indoxyl acetates, being exhibited only by the series 1-methylindoxyl, indoxyl, and thioindoxyl acetates. An interesting feature displayed in Table 2 is the splitting of the CO and C–O–C frequencies in the 4-substituted compounds in carbon disulphide. A likely explanation depends on the assumption that two preferred positions exist for the acetate side-chain. In one of

[11] Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 188; Jaffé, *Chem. Rev.*, 1953, **53**, 191.

these positions (IV), the double-bond character of the carbonyl group is increased by a field effect produced by the propinquity of the 4-substituent.[12]

(d) *Carbonyl Stretching Frequencies of Diacetyl- and 1-Acetyl-indoxyls.*—In diacetylindoxyl (III; R = R'' = Ac, R' = H), one carbonyl group has a position similar to that

TABLE 2. *σ-Values and* C–O–C *and* CO *stretching frequencies* (*cm.*$^{-1}$) *of indoxyl acetates.*

| | | | ν(C–O–C) | | ν(CO) | | |
|---|---|---|---|---|---|---|---|
| Indoxyl acetate | M. p. | $\sigma_{Ph-O}$ | *a* | *c* | *a* | *b* | *c* |
| 4-Cl, 5-Br- | 107° | — | 1223 | 1199 1218 | 1740 | 1750 | 1745 1778 |
| 4 : 5-$Cl_2$- | 95 | — | — | 1201 1217 | — | 1746 | 1745 1777 |
| 4-I- | 216 | — | — | 1192 1222 | — | — | 1741 1768 |
| 4-Cl- | 86 | — | 1220 | 1194 1220 | 1741 | 1747 | 1745 1780 |
| 4-Br- | 107 | — | — | 1191 1225 | — | 1744 | 1743 1770 |
| 7-$CF_3$- | 95 | 0·415 | 1200 | 1204 | 1730 | 1742 | 1758 |
| 5-Br- | 134 | 0·391 | 1227 | 1213 | 1740 | 1742 | 1746 |
| 7-Cl- | 125 | 0·373 | 1220 | 1220 | 1740 | 1740 | 1746 |
| 5-Cl- | 86 | 0·373 | 1226 | 1199 1218 | 1736 | 1740 | 1747 |
| 5-I- | 149 | 0·352 | — | 1207 | — | 1739 | 1747 |
| 7-I- | 84 | 0·352 | — | 1197 1216 | — | 1741 | 1745 |
| 5-F- | 140 | 0·337 | — | 1213 | — | 1740 | 1749 |
| 6-I- | 224 | 0·276 | — | 1213 | — | 1740 | 1749 |
| 6-Br- | 200 | 0·232 | — | 1213 | — | — | 1746 |
| 6-Cl- | 106 | 0·227 | 1220 | 1213 | 1742 | 1742 | 1749 |
| 6-F- | 138 | 0·062 | — | 1213 | — | 1744 | 1749 |
| 5-Me- | 117 | −0·069 | 1223 | 1215 | 1739 | 1736 | 1743 |
| 1-Me- | 61 | — | 1223 | 1220 | 1740 | 1737 | 1742 |
| Indoxyl esters | | | | | | | |
| Acetate | 129 | 0·0 | 1225 | 1213 | 1743 | 1738 | 1743 |
| Propionate | 90 | — | — | 1223 | — | 1744 | 1745 |
| Butyrate | 93 | — | — | — | — | 1745 | — |
| Benzoate | 101 | — | — | 1223 | — | — | 1728 |
| Thioindoxyl acetate | liq. | — | — | 1201 | — | — | 1768 |

Data in columns *a*, *b*, and *c* have been obtained from (*a*) potassium bromide discs, (*b*) chloroform solutions, and (*c*) carbon disulphide solutions respectively. Where blanks occur in these columns, the frequencies have not been measured. All the bands quoted are intense.

TABLE 3. *σ-Values relative to* Ph–N *linkage and* CO *stretching frequencies* (*cm.*$^{-1}$) *of acetanilides, diacetylindoxyls, and 1-acetylindoxyls in chloroform.*

| | | Acetanilides[a] | Diacetylindoxyls | | | *N*-Acetylindoxyls | | |
|---|---|---|---|---|---|---|---|---|
| Subst. | $\sigma_{Ph-N}$ | ν(CO) | M. p. | $\nu_1$(CO) | $\nu_2$(CO) | M. p. | $\nu_1$ (CO) | $\nu_2$(CO) |
| 5-$NO_2$ | 0·778 | — | 220° | 1717 | 1763 | — | — | — |
| 6-$NO_2$ | 0·710 | 1696 | 195 | 1713 | 1757 | — | — | — |
| 4-Cl, 5-Br | 0·600 | — | 167 | 1711 | 1756 | 177° | 1685 | 1721 |
| 6-Br | 0·391 | — | 123 | 1707 | 1752 | 187 | 1681 | 1714 |
| 4-Cl | 0·373 | — | 128 | 1708 | 1753 | 190 | 1681 | 1716 |
| 6-Cl | 0·373 | 1690 | 117 | 1707 | 1751 | 171 | 1680 | 1715 |
| 6-I | 0·352 | 1690 | 124 | 1707 | 1750 | 190 | 1679 | 1715 |
| 5-I | 0·276 | — | 133 | 1707 | 1754 | 200 | 1677 | 1718 |
| 5-Br | 0·232 | — | 124 | 1706 | 1755 | 188 | — | — |
| 5-Cl | 0·227 | 1688 | 130 | 1706 | 1755 | 163 | 1674 | 1719 |
| 6-MeO | 0·115 | 1686 | 145 | 1702 | 1755 | 178 | — | — |
| 5-F | 0·062 | 1685 | 142 | 1700 | 1751 | 148 | 1672 | 1716 |
| None | 0·0 | 1685 | 83 | 1700 | 1751 | 138 | 1673 | 1710 |
| 5-Me | −0·170 | 1682 | 106 | 1696 | 1750 | 156 | 1669 | 1705 |
| 5-MeO | −0·260 | 1678 | 100 | 1692 | 1745 | 170 | 1669 | 1703 |

[a] In relation to the data on substituted acetanilides,[13] position 5 refers to *para*-substitution and positions 4 and 6 to *meta*-substitution.

in acetanilide, and hence substituents in the benzene ring should exert a fairly marked effect on the stretching frequency of this carbonyl group, the frequency shifts being linearly

[12] Bellamy, Thomas, and Williams, *J.*, 1956, 3704; Bellamy and Williams, *J.*, 1957, 861; Jones, Forbes, and Muller, *Canad. J. Chem.*, 1957, **35**, 504.
[13] O'Sullivan and Sadler, *J. Org. Chem.*, 1956, **21**, 1179.

related to the σ value of the substituent with reference to its position relative to the Ph–N linkage ($\sigma_{Ph-N}$). The other carbonyl group is analogous to that in indoxyl acetate and consequently ring substituents R′ should exert a smaller and more erratic effect. Substituted diacetylindoxyls each exhibit two carbonyl stretching frequencies, the lower being the more intense. Comparison of the frequencies with those of acetanilide and with the σ values in Tables 3 and 4 shows that the band near 1700 cm.$^{-1}$ is produced by the *N*-acetyl- and that near 1750 by the *O*-acetyl-carbonyl group. The best values for the 1700 cm.$^{-1}$ band frequencies are given by the regression line $\nu_1 = 1700 + 21{\cdot}4\sigma_{Ph-N}$, the correlation coefficient (*r*) being 0·984. Table 3 shows the absence of correlation between the 1750 cm.$^{-1}$ band frequencies of diacetylindoxyls and $\sigma_{Ph-N}$ values, but the existence of rough correlation with $\sigma_{Ph-C}$ values is demonstrated in Table 4.

TABLE 4. *σ-Values relative to* Ph–C *linkage and upper* CO *stretching frequencies of 1-acetylindoxyls and diacetylindoxyls in chloroform.*

| Substituent | 6-$NO_2$ | 5-$NO_2$ | 4-Cl, 5-Br | 5-Br | 5-Cl | 5-I | 5-F | 4-Cl |
|---|---|---|---|---|---|---|---|---|
| $\sigma_{Ph-C}$ | 0·778 | 0·710 | — | 0·391 | 0·373 | 0·352 | 0·337 | — |
| $\nu_3$(CO) of *N*-acetylindoxyls | — | — | 1721 | — | 1719 | 1718 | 1716 | 1716 |
| $\nu_3$(CO) of diacetylindoxyls | 1757 | 1763 | 1756 | 1755 | 1755 | 1754 | 1751 | 1753 |

| Substituent | 6-I | 6-Br | 6-Cl | 5-MeO | None | 5-Me | 6-MeO |
|---|---|---|---|---|---|---|---|
| $\sigma_{Ph-C}$ | 0·276 | 0·232 | 0·227 | 0·115 | 0·0 | −0·069 | −0·268 |
| $\nu_3$(CO) of *N*-acetylindoxyls | 1715 | 1714 | 1715 | 1703 | 1710 | 1705 | — |
| $\nu_3$(CO) of diacetylindoxyls | 1750 | 1752 | 1751 | 1745 | 1751 | 1750 | 1755 |

1-Acetylindoxyls provide a good example of the use of σ–ν correlations in assigning frequencies to the responsible groups. As shown with substituted isatins,[2,3] an independent double correlation (cross correlation) can occur in the same molecule. Here the lower frequencies of 1-acetylindoxyls correlate well with the $\sigma_{Ph-N}$ values of the substituents (Table 3), and the frequencies of the band near 1715 cm.$^{-1}$ with $\sigma_{Ph-N}$ values (Table 4). The equations of the regression lines for the frequencies are

$$\nu_1 = 1673 + 19{\cdot}4\sigma_{Ph-N} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\nu_3 = 1708 + 26{\cdot}7\sigma_{Ph-N} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and the respective correlation coefficients are 0·966 and 0·972. It is clear from Table 4 that the 5-methoxy-group exerts an anomalous effect on the upper carbonyl frequency of 1-acetylindoxyl and probably a corresponding effect on diacetylindoxyl. The methoxy-group frequently behaves abnormally in σ-correlations and the figures for this group have been omitted in computing equation (2) and its correlation coefficient. Thus the $\nu_1$ bands (Table 3 and equation 1) are produced by stretching vibrations of the *N*-acetyl carbonyl group, and the $\nu_3$ bands (Tables 3, 4, and equation 2) are due to the carbonyl group in position 3.

(e) *Carbonyl Stretching Frequencies of Substituted* N-*Acetyloxindoles and* N-*Acetylisatins.* —An attempt has been made to glean information on the carbonyl bands of acetyloxindoles (V) and acetylisatins (VI). The former are of interest in view of coupling phenomena. Abramovitch [14] has shown that coupling is a common feature in diacyl- and diaroyl-amines possessing reasonable symmetry. Investigation of this feature in oxindoles is complicated by the fact that oxindole itself and some substituted oxindoles [3] possess two well-separated carbonyl bands. Unfortunately, difficulties were encountered in preparing acetyloxindoles, the formation of dyes and other by-products preventing purification of the acetyl derivatives except in three cases. Their carbonyl frequencies (Table 5) increase with

[14] Abramovitch, *J.*, 1957, 1413.

$\sigma_{Ph-N}$ values of the substituents as expected, but the results, by themselves, provide no information on the presence or absence of coupling interaction.

*N*-Acetylisatins, being more readily prepared, were studied in the hope that a triple $\sigma$–$\nu$ correlation might be unravelled and further information on coupling emerge. These

TABLE 5. *Carbonyl stretching frequencies (cm.$^{-1}$) of acetylated oxindoles and isatins in chloroform.*

| Compound | M. p. | $\sigma_{Ph-N}$ | $\nu_1$ | $\nu_2$ | $\nu_3$ |
|---|---|---|---|---|---|
| Isatin | 200° | — | — | 1755 | 1740 |
| *N*-Acetyloxindoles | | | | | |
| 5-Methyl- | 120 | −0·170 | 1708 | 1752 | — |
| (Unsubst.) | 126 | 0·0 | 1710 | 1755 | — |
| 5-Nitro- | 159 | 0·778 | 1720 | 1762 | — |
| *N*-Acetylisatins | | | | | |
| (Unsubst.) | 143 | — | 1721 | 1775 | 1742 |
| 5-Methyl- | 173 | — | 1720 | 1772 | 1735 |
| 5-Methoxy- | 175 | — | 1718 (sh) | 1770 | 1732 |
| 5-Bromo- | 166 | — | 1725 | 1786 | 1745 |
| 4-Chloro- | 167 | — | 1720 (sh) | 1776 | 1730 |
| 6-Chloro- | 182 | — | 1720 (sh) | 1787 | 1740 |
| 4 : 5-Dichloro- | 194 | — | 1722 | 1772 | 1745 |
| 6-Fluoro- | 177 | — | 1721 | 1772 | 1738 |

compounds possess the expected three carbonyl maxima (Table 5), but complex interactions spoil possible $\sigma$–$\nu$ correlations. However, the fundamental frequencies of acetylisatins should be well separated and, therefore, coupling is unlikely. Comparison of the stretching frequencies $\nu_2$ and $\nu_3$ of the α- and β-carbonyl groups of isatin with the carbonyl frequencies of *N*-acetylisatin and 1-acetyloxindole (Table 5) suggests that the bands near 1720, 1775, and 1740 cm.$^{-1}$ in *N*-acetylisatin arise from vibrations of the carbonyl groups in the *N*-acetyl group, and in positions 2 and 3 respectively. In the absence of other evidence, this comparison also suggests that coupled oscillation does not occur in 1-acetyloxindole and that again the lower frequency $\nu_1$ may be referred to the *N*-acetyl group.

## EXPERIMENTAL

*Spectra.*—Compounds were examined consecutively, under identical conditions for each medium, a Perkin-Elmer 21 double-beam recording spectrometer fitted with a rock-salt prism being used.

*Diacetylindoxyls.*—These compounds were prepared by heating the corresponding substituted *o*-carboxylphenylglycines under reflux with acetic anhydride and anhydrous sodium acetate.[15] *Diacetyl-5-methoxyindoxyl* (Found: C, 62·9; H, 5·4; N, 6·3. $C_{13}H_{13}O_4N$ requires C, 63·2; H, 5·3; N, 6·7%) formed needles (from aqueous ethanol). *Diacetyl-6-methoxydindoxyl* (Found: C, 63·1; H, 5·3; N, 6·3%) was obtained as white plates from the same solvent.

*Indoxyl Esters.*—The acetates were obtained from the corresponding diacetylindoxyls by deacetylation, under nitrogen, with boiling aqueous alkali, followed by reacetylation with acetic anhydride under Schotten–Baumann conditions.[15] Indoxyl propionate, butyrate, and benzoate were similarly prepared.

1-Methylindoxyl acetate was obtained from *o*-carboxyphenyl-*N*-methylglycine and boiling acetic anhydride containing anhydrous sodium acetate.[16] In a similar manner (*o*-carboxyphenylthio)acetic acid gave thioindoxyl acetate.[15]

1-*Acetylindoxyls.*—To the corresponding diacetylindoxyl (0·1 g.), in the minimum volume of boiling ethanol, was added hydrated sodium sulphite (0·1 g.) in twice the volume of hot

[15] Holt and Sadler, *Proc. Roy. Soc.*, 1958, *B* (in the press); Holt and Petrow, *J.*, 1947, 611; Schwartz, *Monatsh.*, 1905, **26**, 1253.
[16] Ettinger and Friedländer, *Ber.*, 1912, **45**, 2075.

XUM

water. The mixture was heated under reflux for 10 min. and cooled; the product crystallized from aqueous ethanol giving, in good yield, the appropriate 1-acetylindoxyl as white needles (see Table 6).

N-*Acetylisatins*.—Acetylation of isatins was effected by heating the solids under reflux for 1—2 hr. with excess of acetic anhydride.[17] Crude acetyl derivatives, which separated from the cooled mixtures, were purified by crystallization from acetic acid (charcoal) (see Table 7). 7-Chloro- and 7-nitro-isatin could not be acetylated by this procedure, presumably owing to steric hindrance. M. p.s of 1-acetyl-isatins and -oxindoles are in Table 5.

TABLE 6. N-*Acetylindoxyls*.

| | | Found (%) | | | Required (%) | |
|---|---|---|---|---|---|---|
| | M. p. | C | H | Formula | C | H |
| 5-*Fluoro-* | 148° | 62·0 | 4·6 | $C_{10}H_8O_2NF$ | 62·2 | 4·2 |
| 4-*Chloro-* | 190 | 57·2 | 3·6 | $C_{10}H_8O_2NCl$ | 57·3 | 3·8 |
| 5-*Chloro-* | 163 | 57·4 | 4·0 | $C_{10}H_8O_2NCl$ | 57·3 | 3·8 |
| 6-*Chloro-* | 171 | 57·5 | 4·0 | $C_{10}H_8O_2NCl$ | 57·3 | 3·8 |
| 7-*Chloro-* | 191 | 57·1 | 4·1 | $C_{10}H_8O_2NCl$ | 57·3 | 3·8 |
| 6-*Bromo-* | 187 | 47·7 | 3·5 | $C_{10}H_8O_2NBr$ | 47·3 | 3·2 |
| 6-*Iodo-* | 190 | 40·2 | 3·0 | $C_{10}H_8O_2NI$ | 39·9 | 2·7 |
| 5-*Bromo-4-chloro-* | 177 | 41·9 | 2·4 | $C_{10}H_7O_2NBrCl$ | 41·6 | 2·4 |
| 5-*Methyl-* | 156 | 69·8 | 5·6 | $C_{11}H_{11}O_2N$ | 69·9 | 5·8 |
| 6-*Methoxy-* | 178 | 64·1 | 5·3 | $C_{11}H_{11}O_3N$ | 64·4 | 5·4 |

TABLE 7. N-*Acetylisatins*.

| | | Found (%) | | | Required (%) | |
|---|---|---|---|---|---|---|
| | Appearance | C | H | Formula | C | H |
| 6-*Fluoro-* | Yellow needles | 58·2 | 2·9 | $C_{10}H_6O_3NF$ | 58·0 | 2·9 |
| 4-*Chloro-* | Yellow needles | 53·9 | 3·0 | $C_{10}H_6O_3NCl$ | 53·7 | 2·7 |
| 6-*Chloro-* | Yellow needles | 53·9 | 2·6 | $C_{10}H_6O_3NCl$ | 53·7 | 2·7 |
| 5-*Bromo-* | Orange plates | 44·7 | 2·2 | $C_{10}H_6O_3NBr$ | 44·8 | 2·3 |
| 4 : 5-*Dichloro-* | Thick yellow plates | 46·8 | 1·8 | $C_{10}H_5O_3NCl_2$ | 46·5 | 1·9 |
| 5-*Methyl-* | Orange needles | 64·9 | 4·5 | $C_{10}H_9O_3N$ | 65·0 | 4·5 |
| 5-*Methoxy-* | Yellow needles | 59·8 | 4·4 | $C_{11}H_9O_4N$ | 60·3 | 4·1 |

N-*Acetyloxindoles*.—Attempts were made to prepare a selection of *N*-acetyloxindoles by direct acetylation (Suida [18]) but, owing to dye-formation and other gross contamination, only two, in addition to the previously-described unsubstituted compound, were obtained pure. The *5-methyl compound* (Found: C, 69·5; H, 5·9. $C_{11}H_{11}O_3N$ requires C, 69·8; H, 5·8%) was obtained as white needles from ethanol. Similar purification gave the *5-nitro-compound*, also as white needles (Found: C, 54·5; H. 4·0. $C_{10}H_8O_4N_2$ requires C, 54·5; H, 3·7%).

One of the authors (A. E. K.) thanks the British Empire Cancer Campaign for a Research Fellowship. Two of them (D. G. O'S. and P. W. S.) thank the Department of Scientific and Industrial Research for a special grant aiding the prosecution of this work.

COURTAULD INSTITUTE OF BIOCHEMISTRY,
MIDDLESEX HOSPITAL MEDICAL SCHOOL, LONDON, W.1. [*Received, October 30th*, 1957.]

[17] Camps, *Arch. Pharm.*, 1899, **237**, 687.
[18] Suida, *Ber.*, 1879, **12**, 1327.

XUM

## 241. *Researches on Monolayers. Part VII.*[1] *Reactions of Casein with Dyes and other Aromatic Solutes and their Relation to Adsorption by Protein Fibres.*

By A. Cameron, C. H. Giles, and T. H. MacEwan.

The effect of aromatic sulphonates, including some dyes, upon casein monolayers spread on acid or on buffer solutions near the isoelectric point has been studied. Large dye molecules with a non-ionic polar group at each end have an effect on the film similar to that of tannic acid. Surface-active monobasic dye molecules with weak hydrogen-bonding groups penetrate the film and at high surface pressures increase its solubility. It is suggested that the latter effect may be due to the adsorption of a layer of dimerised dye molecules below the film.

Small sulphonate molecules and disulphonates with weak hydrogen-bonding centres (*e.g.*, anthraquinonedisulphonates) are probably adsorbed beneath the film. The results are used as a basis for the hypothesis that the affinity of monobasic anions for protein fibres arises from their own mutual attraction, which assists them in forming a monolayer or a layer of micelles adsorbed on the fibre, rather than from specific anion–fibre attraction.

The interaction of organic ions with casein monolayers has been investigated to assess the rôle of polar and non-polar forces in the adsorption of dyes by protein fibres. Organic ions of high molecular weight are readily adsorbed by protein fibres, their affinity generally increasing with the size of their organic residue,[2,3] but the source of this affinity has not been precisely defined. It has been suggested that the major contribution to the affinity is non-polar van der Waals attraction by the hydrophobic portions of the protein molecule (see, *e.g.*, ref. 4), and certain experimental results have been interpreted as evidence that hydrogen bonds do not operate between protein fibres and the anions of sulphonated dyes.[5,6] It has however been pointed out also that dye affinity is not as closely related to molecular weight as it would be if only non-polar forces were acting.[7] There is moreover positive evidence in favour of the hypothesis of hydrogen-bond adsorption of many non-ionic organic solutes, and a few ionic ones, by proteins, *e.g*, the action of tanning agents on protein monolayers on water,[8,9] the adsorption of un-ionised or weakly ionised organic solutes by wool,[3] the interaction of serum albumin or casein with simple azo-compounds,[10] the interference of fibrinogen clotting by thrombin caused by the presence of urea and several alcohols,[11] and complex-formation between casein, edestin, or gelatin and several solutes, including anionic dyes, detected by refractometry.[12,13]

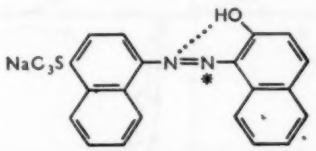
*Previous Work on Dye–Protein Monolayer Interactions.*—A few authors have examined reactions between monolayers and dyes dissolved in the water beneath. Thus Wunderby[14] removed protein monolayers from the surface of solutions of several azo-dyes by lifting them on a glass slide, then redissolved the dye-protein combinations in alkali and examined the solutions spectrophotometrically. He considered that the extent of reaction depended

[1] Part VI, Cameron, Giles, and MacEwan, *J.*, 1957, 4304.
[2] Steinhardt, Fugitt, and Harris, *J. Res. Nat. Bur. Stand.*, 1940, **25**, 219; 1943, **30**, 123.
[3] Vickerstaff, "The Physical Chemistry of Dyeing," Oliver and Boyd, Ltd., Edinburgh, 2nd edn., 1954.
[4] Meggy, *J. Soc. Dyers Colourists*, 1950, **66**, 510.
[5] Derbyshire and Marshall, *Discuss. Faraday Soc.*, 1954, **16**, 140.
[6] Derbyshire, *Trans. Faraday Soc.*, 1955, **51**, 909.
[7] Vickerstaff, *J. Soc. Dyers Colourists*, 1953, **69**, 279.
[8] Schulman and Dogan, *Discuss. Faraday Soc.*, 1954, **16**, 158.
[9] Ellis and Pankhurst, *Discuss. Faraday Soc.*, 1954, **16**, 170.
[10] Klotz and Ayers, *Discuss. Faraday Soc.*, 1953, **13**, 189.
[11] Shulman, *Discuss. Faraday Soc.*, 1953, **13**, 109.
[12] Campbell, Cathcart, and Giles, *J. Soc. Dyers Colourists*, 1957, **73**, 546.
[13] Bruce, Giles, and Jain, *J.*, in the press.
[14] Wunderby, *Experientia*, 1951, **7**, 296.

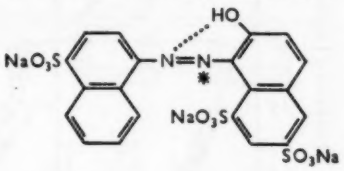
XUM

on the colloidal nature of the dye. While the present work was in progress, Harrap [15] reported experiments on spreading a monolayer of a soluble wool keratin derivative on buffered solutions of Orange II. He observed effects indicating interaction between the protein derivative monolayer and the dye, beyond simple additive penetration. Interaction due to ionic binding occurs below pH 4. At high dye concentrations in the aqueous solution (0·1—0·5M) increased interaction takes place, apparently owing to the dye's being able to aggregate and orient at the surface, and to penetration's being facilitated by the increased screening of negatively charged protein side-chains when the ionic concentration rises.

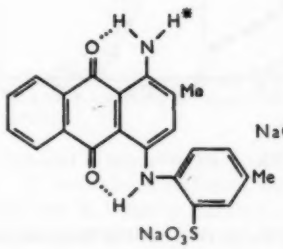
*Present Work.*—The present work was undertaken to define more clearly the source of affinity of organic ions for protein fibres and to resolve some of the apparently conflicting evidence regarding the rôle of polar and non-polar forces in adsorption of dyes by proteins. Surface-pressure and area measurements were made on casein monolayers spread upon water and aqueous solutions of a variety of solutes, including polar non-ionic compounds and a number of aromatic ionic compounds of various molecular sizes and containing different numbers and types of potential hydrogen-bonding group. Non-ionic solutes used were: tannic acid (I), glucose (II), and *m*-inositol (III), and anionic ones were either (i) of small molecular area or with no strongly hydrogen-



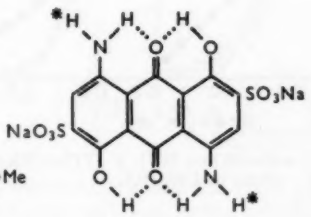
(X) C.I.15620 (ref. 16)



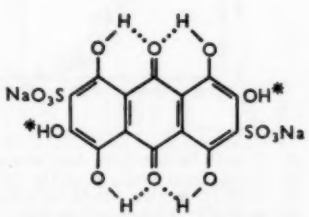
(XI) C.I.16255



(XII) C.I.62085



(XIII) C.I.63010



(XIV) C.I.58610

**The asterisks indicate the probable hydrogen-bonding centres, based in the case of (XII) and (XIII) on direct determination of complex-ratios with phenol in aqueous solution.**

bonding groups [sodium benzenesulphonate (IV), sodium naphthalene-2-sulphonate (V), sodium 2-hydroxynaphthalene-7-sulphonate (F-salt) (VI), and sodium anthraquinone-2-sulphonate (VII) and -1 : 5- and -2 : 7-disulphonates (VIII), (IX); also (XI), (XIII), (XIV)], or (ii) monobasic, having a large hydrophobic residue (*i.e.*, weakly surface-active) [(X), (XII)].

## Results and Discussion

The results are shown in Fig. 1 and the following interpretations are given.

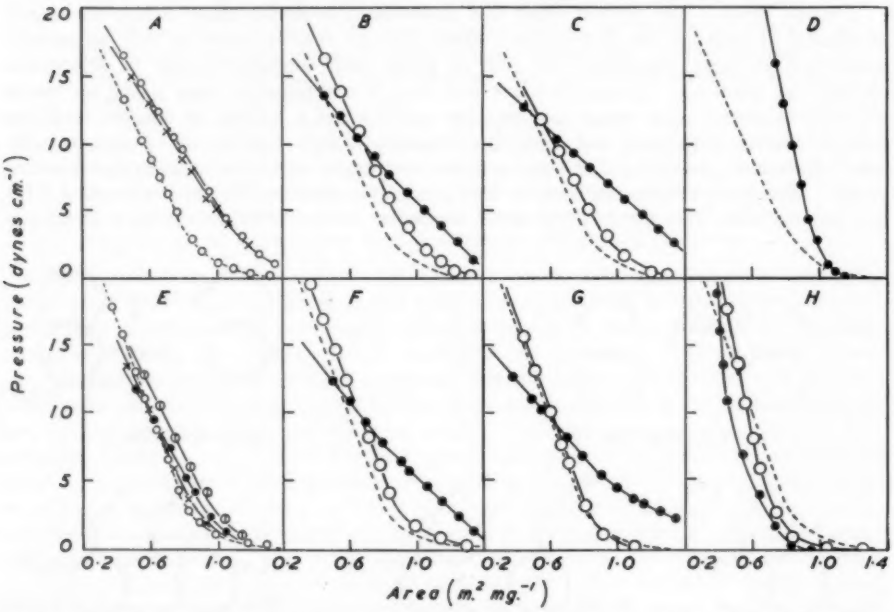
*Effect of Non-ionic Compounds.*—Tannic acid has the same effect upon casein (Fig. 1*H*) as it has on collagen monolayers; [9] it condenses the film, making it more rigid, *i.e.*, less

[15] Harrap, *Proc. Second Internat. Congr. of Surface Activity*, 1957, Preprint, **2**, 370.

[16] "Colour Index," Society of Dyers and Colourists, Bradford, and American Association of Textile Chemists and Colourists, Lowell, Mass., 2nd edn., 1957.

compressible. The hydroxy-groups in the tannic acid molecule form hydrogen bonds with specific groups in a number of protein chains, the whole complex forming a raft-like structure in which the tannic acid molecules lie horizontally in the water below the film. This type of complex can form only with large multifunctional solute molecules [9] and not with the small molecules of glucose and inositol. These compounds (0·01M, pH 4·34) have no apparent effect on the casein film (Fig. 1*E*). Refractometric tests also suggest that they do not form complexes with casein (in alkaline solution).[13]

FIG. 1. *Force–area curves for casein monolayers on water and various substrates.*




*A*; ○ with broken line, Acid alone, ○ with full line, (IV), × (VII)—(IX). All $10^{-3}$M and in 1·0N-HCl.
*B*; ○ (XIII) ($10^{-3}$M), ● (XII) ($10^{-5}$M). Both in 1·0N-HCl.
*C*; ○ (XI), ● (X). Both in 1·0N-HCl.
*D*; ● (XIV) ($10^{-3}$M) in 1·0N-HCl.
*E*; ○ Acid alone, coinciding with (II) and (III) ($10^{-2}$M); ⓘ (V), ● (IX), × (VI). All $10^{-3}$M in buffer pH 4·34.
*F*; ○ (XIII) ($10^{-3}$M); ● (XII) ($10^{-4}$M). Both in buffer pH 5·1.
*G*; ○ (XI), ● (X). Both $10^{-3}$M in buffer pH 5·1.
*H*; ○ (XIV) ($5 \times 10^{-4}$M), ● (I) (43 mg. l.$^{-1}$). Both in buffer pH 4·34.
For comparison the control curve is repeated (broken) in curves *B*—*H*.

*Effect of Anionic Solutes in Acid Solution.*—Hydrochloric acid alone, at pH 1·0, has little effect on the film (Fig. 1*E*), but when an aromatic anionic solute is present considerable expansion occurs, with in most cases some change in compressibility (Fig. 1*A*–*D*). Ellis and Pankhurst [9] found that basic chromium sulphate expands a gelatin monolayer without causing any noticeable change in compressibility and attributed the effect to the action of coulombic forces between the solute ions and oppositely charged side-chains of the protein. The expansion of the present casein films is attributable also to coulombic attraction, but the compressibility changes are probably due to forces acting between the protein and the organic residues of the solute ions in the water below the film (Fig. 2*A*). The expansion may then be the result of the interposition of the solvated water atmospheres around the individual ionic centres.

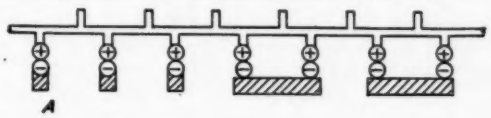
The compressibility of the casein films varies in an interesting manner with the nature of the solute anion, and the variations suggest differences in the location of the attached anions. Three effects can be distinguished.

(i) *Slight increase in compressibility.* This occurs with the small monobasic anion, *i.e.*, sodium benzenesulphonate (Fig. 1*A*), and with the di- or tri-basic anions which have no strongly hydrogen-bonding centres and no very large unsulphonated residue, *i.e.*, the anthraquinonesulphonates (VII—(IX) (Fig. 1*A*) and the azo-dye (XI) (Fig. 1*C*). These have neither surface activity nor cross-linking power, so they must be located in the water just below the film (Fig. 2*A*).

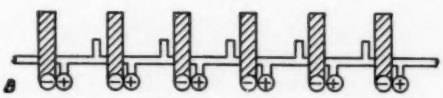
(ii) *Great increase in compressibility.* The two monobasic dyes (X) and (XII) cause considerable increase in film area and compressibility (Fig. 1*C*, *B*). The liquid-expanded type of film obtained resembles those observed when one monomeric surface-active compound penetrates a film of another (cf. ref. 17).* There is clearly ion–ion association between the charged cationic groups of the protein and the dye sulphonate groups. In the greatly expanded state the dye molecules must be lying flat on the surface, their large area causing the protein chains to be widely separated.

FIG. 2. *Schematic diagram of suggested mechanism of casein–dye attachment under acid conditions.*

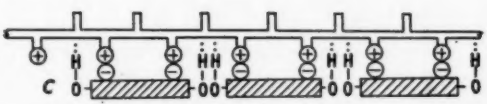
Ion–ion bond with small uni- or bi-valent anions.




Ion–ion bond and film penetration with large univalent anions at moderate pressure.




Ion–ion and hydrogen bonds with bivalent anions containing at least two bonding groups.




It was also found that injection of a solution (final concn. in the trough 0·00004M) of the dye X below a casein film on pH 4·34 buffer, previously compressed at 8 dynes/cm., caused the film to expand to the area obtained at that pressure when it is initially spread on dye solution (cf. Fig. 1*G* and p. 1228). This evidence of penetration of a film of one compound *A* under pressure by another compound *B* injected below it implies that a stable complex is formed between *A* and *B*.[19] The complex appears to be stable over the whole pressure range examined, for the curve for the mixed film intersects that for casein alone at high pressures (Fig. 1*C*). This implies that the film does not return to its normal state under high pressure but remains actually more soluble that it is in the absence of dye, and that therefore sulphonate groups in the complex must be in contact with the water.

The mechanism of association at the higher pressures may well resemble that postulated by Pankhurst [20] for gelatin–sodium alkyl sulphate detergent complexes formed in solution. Under acid conditions the ion–ion attraction causes a monolayer of detergent to be built

* For a general discussion of some effects of penetration of films, see Schulman.[18]

[17] Pankhurst, *Proc. Roy. Soc.*, 1941, **179**, *A*, 393.
[18] Schulman, *ibid.*, 1936, **155**, *A*, 701.
[19] Schulman and Hughes, *Biochem. J.*, 1935, **29**, 1243.
[20] Pankhurst, "Surface Chemistry," Butterworths, London, 1949, p. 109.

up on the protein, with the polar groups oriented towards the protein and the hydrocarbon groups directed outwards, giving the complexes oil-solubility. Further detergent anions are adsorbed in the reverse manner, being attached to the first layer by van der Waals forces between the hydrocarbon chains. A reverse-adsorbed layer of this nature, beneath the casein film, would give the latter a closely-packed surface of sulphonate groups, which would account for its high solubility. The two dyes (X) and (XII) which cause the increased film solubility each have a structure which would favour dimerisation by van der Waals attraction, giving a complex with a sulphonate group at each end. A similar dye (Orange II, sulphanilic acid→2-naphthol) has been shown by Derbyshire [6] to exist in dilute aqueous solution largely in such a form.

At an intermediate stage between the liquid-expanded film and the final state, the aromatic portion of the dye molecules may be forced partially out of the film to stand vertically upwards (Fig. 2*B*). If this does occur, then with increasing compression the orientation of the adsorbed dye molecules may be envisaged as passing through three stages with possible " buckling " of the film in each.

(iii) *No change, or decrease in compressibility.* The anthraquinone dye (XIV) produces a marked decrease in compressibility (Fig. 1*D*), doubtless a " tanning " effect caused by hydrogen-bond cross-linking of protein chains with active phenolic groups at opposite ends of the dye molecule (cf. Fig. 2*C*).* This dye expands films of monomeric non-ionic surface-active substances, by cross-linking,[21,22] but in these monomeric films the compressibility is greatly increased by cross-linking.

The other anthraquinone dye with two hydrogen-bonding centres (XIII) produces no change in film compressibility (Fig. 1*B*). Its effect is thus intermediate between those of, say, (IX) and (XIV), and it is probably causing a small degree of hydrogen-bond cross-linking, the affinity of its bonding centres under acid conditions being low, and only slightly greater than that of the quinone groups.

*Effect of Anionic Compounds near the Isoelectric Point.*—The isoelectric point of casein is at pH 4·6, and on buffer solutions in this region the ion–ion attraction is low and any changes in the films must be due to non-ionic and some ion–dipole forces. The compressibility changes are similar to those observed with acid solutions, but the expansions are less (see Fig. 1*E*).

The form of the curves obtained with the two monobasic dyes (X) and (XII) (Fig. 1*G*, *F*) is very similar to that obtained with these dyes on acid solutions, and a sequence of orientation changes can be suggested to occur here similar to those on acid solutions. Pankhurst [20] observed that the sequence of changes in the properties of detergent–gelatin complexes is much the same above as below pH 2, but in the latter conditions the detergent : protein ratio required to give maximum hydrophobic properties is higher, and some inorganic salt must also be in the solution; the anions are probably first adsorbed at the keto-imide groups in the backbone of the protein, rather than on side-chains. In the present case the buffer gives the required salt effect.

*Nature of Non-ionic Dye–Protein Reactions.*—The present results throw some light on the non-ionic reactions of dyes and other organic ionised solutes with protein fibres and help to reconcile some of the apparently conflicting evidence obtained by earlier investigators. It appears first that non-ionic polar groups in sulphonate anions can form hydrogen bonds to casein in water over quite a wide pH range. In anions with weak hydrogen-bonding power, however, bonding effects with the casein monolayer are masked by other effects produced either by surface activity in " unsymmetrically " sulphonated dyes [*e.g.*, (X) and (XII)] or by high water-solubility in " symmetrically " sulphonated compounds [*e.g.*, (VII)—(IX) and (XI)]. If it is assumed that suitable polar groups are

* The rigidity of the " tanned " film can be seen by sprinkling powdered talc on the surface; the " penetrated " films are markedly less rigid.

[21] Giles and Neustädter, *J.*, 1952, 3806.
[22] Allingham, Giles, and Neustädter, *Discuss. Faraday Soc.*, 1954, **16**, 92.

as accessible in wool as in casein it follows that there can be hydrogen-bond adsorption by that fibre of anions with active polar groups.

From a consideration of the present results and those, for example, of Pankhurst's work on gelatin complexes [20] the known phenomena of anion affinity for wool can be accounted for by the following tentative hypothesis.

The affinity for a protein fibre P of surface-active anions $R{\cdot}SO_3'$, *i.e.*, those having their ionic group or groups at one end of the molecule, and having only weak hydrogen-bonding power, *arises from the mutual forces between the anions themselves, i.e.*, the forces (largely van der Waals forces) between R and R, rather than between R and P. These mutual forces assist the adsorbed anions to form either a condensed monolayer or micelles. Evidence in favour of this suggestion is: (i) The rise in affinity for wool of monobasic aromatic anions with increase in their molecular size [3, 7] (the affinity of some dyes rises linearly with increase in length of an attached alkyl chain). If the affinity were due to R–P attraction it would be unlikely to rise regularly with size of R, because the protein molecule would become more and more inaccessible to the anions as they increased in size (cf. ref. 23). (ii) The similarity in heat of reaction in water of the dye Orange II (as the free acid) with wool (−9·27 kcal./mole) and (as the sodium salt) with itself (−10·48 kcal./mole).[6] If the reaction were between the dye anion and hydrophobic parts of the protein molecule the " heat of dyeing " would be expected to differ from the heat of dimerisation, *e.g.*, the heat of reaction of the dye anion with several amino-acids, even including tyrosine, whose side-chain, being aromatic, is nearest in type to the dye itself, is only about −1 kcal./mole.[5] (iii) The behaviour of a monolayer of long-chain alkyl sulphate ($C_{22}H_{45}SO_4Na$) when a protein (hæmoglobin) is injected beneath it. No penetration occurs at the isoelectric point of the protein, but it does occur under acid conditions, where ion–ion attraction between sulphate and protein is powerful enough to expand the film.[24] This suggests that the attraction of one alkyl chain for another in the condensed monolayer is greater than its attraction for the protein. (iv) The character of the surface of wool dyed with surface-active sulphonated dyes containing paraffin chains. A brief report by Preston [25] is that when dyed under acid conditions the fibre surface is hydrophobic and when dyed neutral it is hydrophilic. In acid solution sulphonate groups of the dye are attached to the charged groups in the fibre and the alkyl chains directed outwards; in neutral solution the sulphonate groups are not attracted by the uncharged fibre, but are directed towards the water. These observations suggest that the dye anions on the the fibre surface, in both sets of conditions, are present either in a condensed monolayer oriented perpendicular to the surface, or in micelles. The mutual attraction between the hydrophobic portions of the anions themselves must therefore be greater than their attraction for the hydrophobic parts of the wool molecule.

The affinity of non-surface-active anions for protein must arise largely from dye–protein attraction, due partly to hydrogen-bond forces and partly to van der Waals attraction, but the quantitative data available are inadequate to confirm this point.

*Hydrogen-bonding and Interanion Attraction with Dissolved and Fibrous Proteins.*—A surface-active ion with weak hydrogen-bonding centres may form hydrogen-bonded complexes with proteins when both are in solution, but at a solid protein surface it may be adsorbed so that the aromatic residues of the dye ion are associated with themselves alone and not hydrogen-bonded to the protein. This explains why casein–surface-active dye hydrogen-bonded complexes appear to exist in solution (at least in alkaline solution *) [12] but not always when the dye is adsorbed at the casein monolayer.

* Calorimetric measurements give no evidence of hydrogen-bond interaction between amino-acids or dipeptides and the free acid of Orange II in very low concentration in acid solution.[5] Under these conditions the ion–ion reaction must preponderate over the competing dipole–dipole (hydrogen-bond) reaction.

[23] Pankhurst, *Discuss. Faraday Soc.*, 1949, **6**, 52.
[24] Matalon and Schulman, *Discuss. Faraday Soc.*, 1949, **6**, 27.
[25] Preston, *Hexagon Digest*, 1952, No. 11, 31.

*Experimental.*—The apparatus has been described.[1] The dyes and other reagents were purified by normal methods and were dissolved in distilled water. Casein was B.D.H. " light white soluble " quality, spread from a 0·15% solution in pH 9 buffer by dropping on the water surface from an " Agla " micrometer syringe. Preliminary tests showed that the film reached equilibrium in about 15 min., but in each case after spreading 30 min. were allowed before the film was compressed. Subsequent stages of compression were measured after intervals of 3 min., which was sufficient to allow the film to regain equilibrium. During this time the pressure decreases slightly, possibly owing to reorientation of side-chains.

The authors thank Professor P. D. Ritchie for his encouragement and interest; the Wool Textile Research Council for a scholarship (to A. C.) and a grant; the D.S.I.R. for a scholarship (to T. H. MacE.); and Dr. M. A. T. Rogers and Imperial Chemical Industries Limited, Dyestuffs Division, for the gift of dyes and intermediates.

Department of Chemical Technology,
Royal College of Science and Technology,
Glasgow, C.1.

[*Received, October 30th,* 1957.]

---

## 242. *Chalcones and Related Compounds. Part IV.* Addition of Hydrogen Cyanide to Chalcones.*

By W. Davey and D. J. Tivey.

The optimum preparative conditions for chalcones have been confirmed and some new chalcones prepared. Improvements have been effected in the addition of hydrogen cyanide to chalcones and in the hydrolysis of the resulting adducts. New lactones, pyridazinones, and diols have been prepared from these adducts.

Although sodium hydroxide is usually assumed to be the preferred reagent for the condensation of benzaldehydes with acetophenones, few attempts have been made to compare accurately the efficacy of various condensing agents. Comparative experiments have shown that sodium hydroxide and sodium methoxide are generally more effective than hydrogen chloride, phosphorus oxychloride, or boron trifluoride in the preparation of chalcone and of some twelve substituted chalcones. The experimental procedures and the results obtained are detailed later and the preparation of some new chalcones is described.

Treatment of chalcone with potassium cyanide and acetic acid yields 3-cyano-1 : 3-diphenylpropan-1-one (I) and a sparingly soluble product (II) by further addition.[1,2,3] Although some improvements in the yield of adduct (I) have been obtained [4,5] and the

(I) $Ph{\cdot}CH(CN){\cdot}CH_2{\cdot}COPh$ $\qquad$ $Ph{\cdot}CH(C(CN){\cdot}CH_2{\cdot}COPh){\cdot}CH_2{\cdot}COPh$ (II)

method extended to some other chalcones,[6] some workers [7,8] have recorded difficulties in the reaction or failure in some cases. Although Allan and Kimball's method [5] was found satisfactory for the addition of hydrogen cyanide to chalcone and to 4-methoxychalcone, it failed with 4'-methoxy-, 4 : 4'-dimethoxy-, and 4'-hydroxy-chalcone. Variations in reaction temperature and amounts of potassium cyanide and acetic acid had little effect

* Part III, *J.*, 1957, 1017.

[1] Anschütz and Montfort, *Annalen*, 1895, **284**, 2.
[2] Rupe and Schneider, *Ber.*, 1895, **28**, 960.
[3] Hann and Lapworth, *J.*, 1904, **85**, 1355.
[4] Lapworth and Wechsler, *J.*, 1910, **97**, 39.
[5] Allan and Kimball, *Org. Synth.*, Coll. Vol. II, p. 498.
[6] Robertson and Stephen, *J.*, 1931, 863.
[7] Kohler and Leers, *J. Amer. Chem. Soc.*, 1934, **56**, 981.
[8] Mehta *et al.*, *J. Univ. Bombay*, 1942, **10**, 137; 1940, **9**, 156.

on yield, and addition of hydrochloric acid gave tars. Addition of hydrogen cyanide to chalcones in the presence of sulphuric acid and ethanol gave high yields of adducts free from secondary reaction products. Although the amount of acid was not critical, the best results were obtained when the acid and potassium cyanide were used in a molar ratio of 1 : 2. The required adducts were obtained from chalcone, 4'-methoxy-, 4 : 4'-dimethoxy-, 3 : 4 : 4'-trimethoxy-, and 2 : 4 : 4'-trimethoxy-chalcone.

Acid hydrolysis of the 3-cyano-1 : 3-diarylpropan-1-ones to the corresponding acids is difficult [1, 3, 9] and after such hydrolysis the 2 : 4-diaryl-4-oxobutanoic acids tended to separate as oils. Conversion of the cyano-ketones into methyl esters by boiling them with methanolic hydrogen chloride, followed by hydrolysis with dilute sodium hydroxide, gave the acids in good yield.

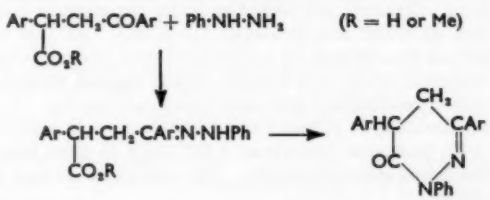
1 : 3-Diarylbutane-1 : 4-diols have not been previously prepared and it appeared that the reduction of esters of the 2 : 4-diaryl-4-oxobutanoic acids by lithium aluminium hydride should give such compounds:

$$MeO_2C{\cdot}CHAr{\cdot}CH_2{\cdot}COAr \longrightarrow HO{\cdot}CH_2{\cdot}CHAr{\cdot}CH_2{\cdot}CHAr{\cdot}OH$$

The keto-esters and -acids already contain one asymmetric carbon atom and, on reduction of the keto-group, a second asymmetric carbon atom will be produced, giving rise to two stereoisomers (*threo* and *erythro*), each being a racemate. Reduction occurred readily to yield the diols as low-melting solids or oils. Since the keto-esters were sparingly soluble in ether, reduction was carried out either by ethereal lithium aluminium hydride in a Soxhlet apparatus with the keto-ester in the thimble, or by the addition of a benzene solution of the ester to ethereal lithium aluminium hydride.

Reduction of 4-oxo-2 : 4-diphenylbutanoic acid with sodium in ethanol gave 4-hydroxy-2 : 4-diphenylbutanoic lactone. It was thought possible that reduction by potassium borohydride, or catalytically, of esters of 4-oxo-2 : 4-diarylbutanoic acids would give the corresponding hydroxy-esters and avoid lactone formation but, in fact, potassium borohydride gave the lactone. Catalytic hydrogenation in presence of a Raney nickel W.7 catalyst was used to avoid lactonisation and a syrup having the correct analysis obtained. Since it was presumably a mixture of stereoisomers an attempt was made to separate it chromatographically but without success. Alkaline hydrolysis or vacuum-fractionation of the syrup gave the saturated lactone. Reduction of other keto-esters by potassium borohydride gave saturated lactones in good and reproducible yields.

The action of phenylhydrazine in γ-keto-acids yields tetrahydro-oxopyridazines,[1] and such compounds were readily obtained by treatment of 4-oxo-2 : 4-diarylbutanoic acids or their methyl esters, with phenylhydrazine in hot glacial acetic acid:

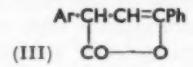



The infrared spectrum of a di-(*p*-methoxyphenyl)pyridazine derivative showed peaks at 1696 (amide-carbonyl group in a six-membered ring), 1514 (conjugated C:N⁻ attached to N), and at 1490 and 1601 cm.$^{-1}$, both characteristic of the aromatic systems. Such analysis confirms the above structure for such compounds.

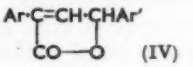
The formation of butenolactones from diaryloxobutanoic acids has been described [1, 3, 4, 6] and two isomeric forms have been reported. The low-melting form was assigned the structure (III) and the high-melting form the structure (IV). The insolubility of the

[9] Rupe and Gisiger, *Helv. Chim. Acta*, 1925, **8**, 338.

latter and the wide difference in m. p.s suggested that isomer (IV) might be a dimer and the problem was investigated in detail.




(III)




(IV)

Treatment of 4-oxo-2 : 4-diphenylbutanoic acid with acetic anhydride gave a good yield of the low-melting form, with a small amount of the other. Heating the low-melting form in ethanol or acetic acid for long periods gave only small amounts of the other form, and prolonged heating of the keto-acid above its m. p. gave a small amount of high-melting lactone and much unchanged acid. The action of acetic anhydride on three other keto-acids gave high- and low-melting lactones, the former in very small yield. The low-melting lactones had m. p. *ca.* 100° and were soluble in most common solvents whilst the high-melting forms were extremely insoluble in solvents and had m. p. *ca.* 300°. Molecular-weight determinations by the Rast method confirmed the monomeric nature of the low-melting lactones and, although results were poor for the sparingly soluble high-melting forms, some evidence of their monomeric nature was obtained. Repeated analyses confirmed the formulæ for unsaturated lactones. Catalytic hydrogenation of the low-melting isomer gave αγ-diphenylbutyric acid in high yield. The infrared spectra of both forms provided little evidence since, owing to the insolubility of the high-melting form, determinations were on Nujol mull and not on solutions. The high-melting lactone from 2 : 4-di-(*p*-methoxyphenyl)-4-oxobutanoic acid showed a band at 1763 cm.$^{-1}$ which is rather low for a carbonyl group in a five-membered ring lactone, but it is higher than the corresponding band for the low-melting isomer (1750 cm.$^{-1}$) and is slight evidence that the latter is 4-hydroxy-2 : 4-di-(*p*-methoxyphenyl)but-2-enoic lactone. The infrared spectra of the other lactones were even less conclusive, but, in spite of the wide differences in m. p. and solubility, there is no reason to suppose that the high-melting lactones are other than simple isomers of the low-melting forms.

## Experimental

*Preparation of Chalcones* (see Table).—(*a*) This was Kohler and Chadwell's method,[10] the aldehyde and ketone in aqueous ethanol being condensed by sodium hydroxide.

(*b*) The benzaldehyde (1 mol.) and acetophenone (1 mol.) were mixed at 25° and, if either or both were solid, enough ethanol added to make the mixture homogeneous at 30°. 5N-Sodium hydroxide was then added in an amount 10% more than that required to make the mixture distinctly alkaline to "Brilliant Yellow." External cooling kept the mixture at 25—30° and water usually separated. Ethanol was added to make the mixture homogeneous and this procedure repeated as long as water was produced (½—5 hr.). At this stage crystallisation usually began and the product was filtered off and washed with water. Dilution of the filtrate and seeding gave more chalcone, which was filtered off and washed with water. The product was generally pure and one crystallisation gave the required chalcone.

(*c*) A mixture of the benzaldehyde (1 mol.) and acetophenone (1 mol.) in acetic anhydride (200 ml.) was saturated with hydrogen chloride at > +30°, kept at room temperature for 12 hr., then poured into dilute ammonia solution and ice. The separated oil was then steam-distilled and the residue recrystallised.

(*d*) To a mixture of benzaldehyde (1 mol.) and acetophenone (1 mol.), liquefied if necessary by addition of benzene, a few drops of phosphorus oxychloride were added at 30° and the whole was kept at room temperature for some hours. The product was washed with 2N-ammonia, then water, and, after removal of the benzene under reduced pressure, steam-distilled, and the residue recrystallised.

(*e*) The benzaldehyde (1 mol.) was treated with a 48% solution of boron trifluoride (1 mol.) in acetic acid at 25°, enough acid being added to dissolve the aldehyde. Acetophenone (1 mol.) was then slowly added, the temperature being kept at 25—30°. The mixture became red and

[10] Kohler and Chadwell, *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 78.

after 12 hr. at room temperature was treated with excess of sodium acetate solution, then steam-distilled, and the product repeatedly recrystallised.

(*f*) The benzaldehyde (1 mol.) in dry methanol (200 ml.) was added at 30° to a solution of sodium methoxide (from 10 g. of sodium in 100 ml. of methanol), and the acetophenone (1 mol.)

*Chalcone.*

| | (*a*) | (*b*) | (*c*) | (*d*) | (*e*) | (*f*) |
|---|---|---|---|---|---|---|
| Yield (%) | 89 | 76 | 50 | 48 | 53 | 71 |
| Reaction time (hr.) | 2 | 1 | 12 | 12 | 6 | 4 |
| M. p. (no. of crystns. in parentheses) | 52° (1) | 55° (0) | 53° (2) | 52° (2) | 52° (2) | 52° (1) |

Kohler and Chadwell [10] report m. p. 55° and 98% yield by method (*a*).

*Substituted chalcones*: *yields* (*m. p.s in parentheses*).

| Subst. | (*b*) | (*c*) | (*d*) | (*e*) | (*f*) |
|---|---|---|---|---|---|
| 4-MeO [a] | 76 (75) | 50 (72) | 47 (73) | 52 (70) | 61 (72) |
| 4 : 4′-$(MeO)_2$ [b] | 81 (100) | 66 (99) | 50 (100) | 62 (97) | 75 (98) |
| 4-MeO-4′-Me [c] | 55 (91) | — | — | — | 48 (91) |
| 3′-HO [d] | 41 (124) | Tar | Tar | 10 (123) | 35 (123) |
| 4 : 4′-$Me_2$ [e] | 76 (126) | 70 (124) | — | — | 77 (126) |
| 4-Me [f] | 42 (94) | 30 (95·5) | 20 (96) | — | 45 (95) |
| 4-HO [g] | 37 (180) | 11 (182) | 20 (179) | 25 (179) | 31 (182) |
| 4′-MeO [h] | 81 (106) | 55 (105) | 45 (104) | — | 77 (108) |
| 4-$NO_2$ [i] | 60 (162) | 80 (162) | 42 (162) | 35 (162) | 57 (162) |
| 3′-$NO_2$ [j] | 75 (130) | 25 (131) | 10 (130) | — | Tar |
| 4′-Me [k] | 35 (75) | 42 (75) | 22 (72) | 23 (72) | — |

[a] Kohler and Conant, *J. Amer. Chem. Soc.*, 1917, **39**, 1709, used NaOH and gave m. p. 77°, 85% yield. [b] Straus, *Annalen*, 1910, **374**, 139 (NaOEt–EtOH), gives m. p. 101°, 84% yield. [c] Stobbe, *J. prakt. Chem.*, 1929, **123**, 241 (NaOEt–EtOH), gives m. p. 94°, 45% yield. [d] Kostanecki and Tambor, *Ber.*, 1899, **32**, 1924 (NaOH), give m. p. 126°, yield not stated. [e] Weygand, *Annalen*, 1926, **449**, 29 (NaOMe–MeOH), gives m. p. 127—128°, 82% yield. [f] Weygand, *Ber.*, 1927, **60**, 2431 (NaOH), gives m. p. 96·5°, yield not stated. [g] Sablich, *Ber.*, 1896, **29**, 236, gives m. p. 182, yield not stated. [h] Staudinger and Kon, *Annalen*, 1911, **384**, 123 (NaOH), give m. p. 106—107° and 83% yield. [i] Le Fèvre, Markham, and Pearson, *J.*, 1933, 344 (HCl), give m. p. 164°, 86% yield. [j] Le Fèvre, Markham, and Pearson (*loc. cit.*) (NaOMe–MeOH), give m. p. 131°, 33% yield. [k] Weygand, *Annalen*, 1926, **449**, 29 (NaOH), gives m. p. 75°, yield not stated.

added. After some hours at room temperature the separated chalcone was filtered off and washed with water, and the filtrate diluted with water and set aside, more chalcone separating. The product was then recrystallised.

2-*Chloro*-4′-*methylchalcone*.—To 2-chlorobenzaldehyde (14·1 g., 0·1 mole) and 4-methylacetophenone (13·4 g., 0·1 mole) in 96% ethanol (150 ml.) at 30°, 20% sodium hydroxide solution (5 ml.) was added. After 30 min. water separated and more ethanol was added to make the mixture homogeneous. This procedure was repeated during 1½ hr., crystallisation then beginning. Addition of water (15 ml.) and storage at 0° for 3 hr. gave 2-*chloro*-4′-*methylchalcone* (14·6 g., 57%), plates (from ethanol), m. p. 78° (Found: C, 74·9; H, 5·1; Cl, 13·9. $C_{16}H_{13}OCl$ requires C, 74·6; H, 4·9; Cl, 13·8%).

3-*Hydroxy*-4′-*methoxychalcone*.—*m*-Hydroxybenzaldehyde (12·2 g.) and 4-methoxyacetophenone (15·0 g.) were condensed in ethanol by method (*b*), to give 3-*hydroxy*-4′-*methoxychalcone* (18·8 g., 74%), needles (from ethanol), m. p. 160—161° (Found: C, 75·5; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·6%).

3 : 4′-*Dimethylchalcone*.—*m*-Tolualdehyde (12·0 g.) with 4-methylacetophenone (13·4 g.) in ethanol by method (*b*) gave 3 : 4′-*dimethylchalcone* (8·5 g. 36%), as yellow plates (from methanol), m. p. 84° (Found: C, 86·1; H, 6·8. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%).

2 : 4′-*Dimethylchalcone*.—*o*-Tolualdehyde (12·0 g.) with 4-methylacetophenone (13·4 g.) in ethanol by method (*b*) gave 2 : 4′-*dimethylchalcone* (7·1 g., 30%), yellow plates (from ethanol), m. p. 38—40° (Found: C, 86·8; H, 6·7. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%).

2-*Chloro*-4′-*methoxy-chalcone*.—*o*-Chlorobenzaldehyde (14·1 g.) with 4-methoxyacetophenone (15·0 g.) in ethanol by method (*b*) gave 2-*chloro*-4′-*methoxychalcone* (15·3 g., 64%), white plates (from ethanol), m. p. 89—90° (Found: C, 70·0; H, 4·8. $C_{16}H_{13}O_2Cl$ requires C, 70·4; H, 4·8%).

*Addition of Hydrogen Cyanide*.—(1) By the method of Allan and Kimball [8] hydrogen cyanide was added to chalcone and to 4-methoxychalcone.

XUM

(2) Kohler and Leers's method [7] gave a low yield of the hydrogen cyanide adduct of 4′-methoxychalcone and the reaction failed with 4 : 4′-dimethoxychalcone.

(3) 7N-Sulphuric acid (50 ml.) was slowly added to a cooled and stirred solution of chalcone (41·6 g.) in ethanol (700 ml.), the mixture was heated to 50°, and potassium cyanide solution (50 g. in 80 ml. of water) was slowly added. The mixture was refluxed for 5 min., then diluted with water (200 ml.), and set aside at room temperature for 12 hr. The precipitated solid was filtered off and extracted with boiling ethanol (3 × 100 ml.). The product from the extract, when recrystallised from ethanol, gave 3-cyano-1 : 3-diphenylpropan-1-one (35 g. 74%), white needles, m. p. and mixed m. p. 126° (Found: C, 81·4; H, 5·7. Calc. for $C_{16}H_{13}ON$: C, 81·7; H, 5·5%).

By this method the following adducts were obtained: 3-cyano-1-*p*-methoxyphenyl-3-phenylpropan-1-one, white needles (86%), m. p. 65° (Kohler and Leers [7] give m. p. 65°); 3-*cyano*-1 : 3-*di*-p-*methoxyphenylpropan*-1-*one*, white needles (from ethanol) (66%, m. p. 113—114° (Found: C, 73·5; H, 6·0; N, 5·0. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8; N, 4·7%); 3-*cyano*-3-p-*hydroxyphenyl*-1-*phenylpropan*-1-*one* (from ethanol) (68%), m. p. 173° (Found: C, 76·5; H, 4·9; N, 5·3. $C_{16}H_{13}O_2N$ requires C, 76·5; H, 5·2; N, 5·6%); 3-*cyano*-3-(2 : 4-*dimethoxyphenyl*)-1-p-*methoxyphenylpropan*-1-*one*, colourless needles (83%), m. p. 125—126° (Found: 69·8; H, 5·4; N, 4·0. $C_{19}H_{19}O_4N$ requires C, 70·2; H, 5·8; N, 4·3%); 3-*cyano*-3-(3 : 4-*dimethoxyphenyl*)-1-p-*methoxyphenylpropan*-1-*one*, needles (79%), m. p. 105° (Found: C, 69·8; H, 5·3; N, 4·1. $C_{19}H_{19}O_4N$ requires C, 70·2; H, 5·8; N, 4·3%).

*Preparation of Methyl Esters from Hydrogen Cyanide Adducts.*—A suspension of 3-cyano-1 : 3-diphenylpropan-1-one (23·5 g.) in methanol (200 ml.) was saturated with dry hydrogen chloride at 25°, refluxed for 1½ hr., about half of the methanol distilled off, and water (200 ml.) added. After being kept overnight at room temperature the product was filtered off and recrystallised from methanol, to yield *methyl* 4-*oxo*-2 : 4 *diphenylbutanoate*, needles, (24 g.), m. p. 103° (Found: C, 75·8; H, 5·7. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%).

From the corresponding adducts the following esters were prepared by this method: *methyl* 4-*oxo*-4-p-*methoxyphenyl*-2-*phenylbutanoate*, plates (91%), m. p. 96° (Kohler and Leers [7] give m. p. 97°); *methyl* 2 : 4-*di*-p-*methoxyphenyl*-4-*oxobutanoate*, needles (from methanol; 85% yield), m. p. 96—97° (Found: C, 69·1; H, 6·2. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·1%); *methyl* 2-p-*hydroxyphenyl*-4-*oxo*-4-*phenylbutanoate*, needles (83%), m. p. 143—144° (Found: C, 71·6; H, 5·5. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6%); *methyl* 2-(2 : 4-*dimethoxyphenyl*)-4-p-*methoxyphenyl*-4-*oxobutanoate*, needles (from ethanol; 83%), m. p. 128—129° (Found: C, 66·8; H, 6·3. $C_{20}H_{22}O_6$ requires C, 67·0; H, 6·1%); *methyl* 2-(3 : 4-*dimethoxyphenyl*)-4-p-*methoxyphenyl*-4-*oxobutanoate*, needles (from methanol; 73%), m. p. 74—75° (Found: C, 67·2; H, 6·3. $C_{20}H_{22}O_6$ requires C, 67·0; H, 6·1%).

*Hydrolysis of Methyl Esters.*—Methyl 4-oxo-2 : 4-diphenylbutanoate (26·8 g.) was refluxed for 2 hr. with ethanol (100 ml.) and 2N-sodium hydroxide (100 ml.). Excess of 2N-hydrochloric acid (120 ml.) was added and the mixture set aside overnight at room temperature. The precipitated acid was filtered off and recrystallised from ethanol, to give 4-oxo-2 : 4-diphenylbutanoic acid, needles (23 g., 80%), m. p. and mixed m. p. 152°. The following acids (all needles) were obtained by the same method: 4-*p*-methoxyphenyl-4-oxo-2-phenylbutanoic acid (93%), m. p. 139—140° (Kohler and Leers [7] give m. p. 141°); 2 : 4-*di*-p-*methoxyphenyl*-4-*oxobutanoic acid* (from ethanol; 91%), m. p. 163—164° (Found: C, 68·5; H, 5·9. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·9%); 2-p-*hydroxyphenyl*-4-*oxo*-4-*phenylbutanoic acid* (from methanol; 83%), m. p. 143—144° (Found: C, 69·8; H, 5·0. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%); 2-(2 : 4-*dimethoxyphenyl*)-4-p-*methoxyphenyl*-4-*oxobutanoic acid* (from ethanol; 80%), m. p. 127—128° (Found: C, 66·1; H, 5·4. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%); 2-(3 : 4-*dimethoxyphenyl*)-4-(p-*methoxyphenyl*)-4-*oxobutanoic acid* as colourless needles from ethanol, yield 80%, m. p. 179—180° (Found: C, 66·1; H, 5·7. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%).

*Preparation of Unsaturated Lactones.*—4-Oxo-2 : 4-diphenylbutanoic acid (12·7 g.) was refluxed for 3 hr. in acetic anhydride (25 ml.), cooled, poured into cold water, and set aside for 1 hr. The solid was filtered off. The crude product (10 g.) was dissolved in boiling ethanol (50 ml.), filtered hot and, on cooling, gave colourless needles (2·6 g.), m. p. 199°. Dilution of the filtrate with water (15 ml.) gave a solid which was filtered off and dried (6·1 g.; m. p. 91°). The higher-melting product was twice crystallised from ethanol, to yield 4-hydroxy-2 : 4-diphenylbut-2-enoic lactone (1·7 g.; m. p. 283—285°), whilst the lower-melting material, after two crystallisations from ethanol, gave 4-hydroxy-2 : 4-diphenylbut-3-enoic lactone, as

XUM

colourless needles (3·7 g.; m. p. 107—108°). Anschutz and Montfort [1] give m. p. 109° and 288°. It was found that the reflux time with acetic anhydride was critical, excessive refluxing yielding intractable gums. Examples of pairs of isomeric *lactones* (all colourless needles) with reflux times are given in the Table.

**2 : 4-*Diaryl*-4-*hydroxybut*-2- (IV) *and* -3-*enoic lactones* (III).**

| Reflux (hr.) | 2-Ar | 4-Ar′ | | M. p. | Found (%) C | Found (%) H | Formula | Required (%) C | Required (%) H |
|---|---|---|---|---|---|---|---|---|---|
| 2 | Ph | *p*-MeO·C$_6$H$_4$ | (IV) | 250—260° * | 76·5 | 5·2 | C$_{17}$H$_{16}$O$_3$ | 76·7 | 5·3 |
| | | | (III) | 92 | 76·4 | 5·5 | | | |
| 1·5 | *p*-MeO·C$_6$H$_4$ | *p*-MeO·C$_6$H$_4$ | (IV) | 255—260 * | 72·5 | 5·1 | C$_{18}$H$_{18}$O$_4$ | 73·0 | 5·4 |
| | | | (III) | 106—107 | 73·2 | 5·1 | | | |
| 1 | *p*-HO·C$_6$H$_4$ | Ph | (IV) | 282—284 * | 75·8 | 4·7 | C$_{16}$H$_{14}$O$_3$ | 76·2 | 4·8 |
| | | | (III) | 131—132 | 75·9 | 4·6 | | | |

* With decomp.

*Effect of Heat on* 4-*Oxo*-2 : 4-*diphenylbutanoic Acid*.—The acid (5 g.) was heated to 165° for 2 hr., cooled, and dissolved in boiling ethanol (30 ml.); the mixture was filtered and the filtrate allowed to crystallise. The crystals (0·5 g.) had m. p. 270—280°, and on recrystallisation from ethanol gave 4-hydroxy-2 : 4-diphenylbut-2-enoic lactone (0·2 g.; m. p. 282—284°). The filtrate on concentration yielded, after two recrystallisations from ethanol, 4-hydroxy-2 : 4-diphenylbut-3-enoic lactone (3·7 g.), m. p. 107—108° (*M*, 229. Calc.: *M*, 236).

*Hydrogenation of* 4-*Hydroxy*-2 : 4-*diphenylbut*-3-*enoic Lactone*.—The lactone (2 g.) was hydrogenated in ethanol (25 ml.) in presence of 10% palladised charcoal (0·5 g.), rapid hydrogen uptake (2 mol.) occurring. After filtration and dilution with water, the resulting oil was extracted with 2N-sodium carbonate (3 × 20 ml.), and the carbonate solution extracted with ether (2 × 20 ml.) and acidified with hydrochloric acid. The resulting oil was extracted with ether (2 × 20 ml.), the ether removed under reduced pressure, and the product crystallised from light petroleum (b. p. 40—60°), to give αγ-diphenylbutyric acid (1·5 g., 60%), m. p. 73—74° (Found: C, 80·3; H, 6·8. Calc. for C$_{16}$H$_{16}$O$_2$: C, 80·0; H, 6·7%). Bergmann [11] gives m. p. 75°. An attempt to hydrogenate the high-melting lactone was not successful owing to insolubility of the compound.

*Preparation of Saturated Lactones*.—(*a*) Methyl 4-oxo-2 : 4-diphenylbutanoate (5 g.) in ethanol (50 ml.) was added slowly to a stirred solution of potassium borohydride (2 g.) in water (5 ml.) and ethanol (95 ml.) and kept at room temperature for 5 hr., then evaporated to one-fifth of its volume and acidified with hydrochloric acid. The resulting green viscous syrup was taken up in benzene and the benzene distilled off, to give an oil which solidified after 4 days. Recrystallisation from ethanol gave 4-hydroxy-2 : 4-diphenylbutanoic lactone as needles (3·5 g., 80%), m. p. 102°. Anschütz and Montford [1] give m. p. 103—104°.

(*b*) Methyl 4-oxo-2 : 4-diphenylbutanoate (4 g.) in ethanol (50 ml.) was shaken with Raney nickel W. 7(1 g.) and hydrogen until 1 mol. (337 ml.) was absorbed. After filtration and evaporation the syrup (4 g.) was distilled under reduced pressure (b. p. 190—200°/2 mm.) to give the lactone (2·8 g., 85%), m. p. 96°, rising to 102° on crystallisation from light petroleum (b. p. 40—60°). This was identical with that obtained as in (*a*).

By method (*a*) were obtained 4-*hydroxy*-4-p-*methoxyphenyl*-2-*phenylbutanoic lactone* plates (from ethanol) (62%), m. p. 77° (Found: C, 76·4; H, 5·9. C$_{17}$H$_{16}$O$_3$ requires C, 76·1; H, 6·0%), and 4-*hydroxy*-2 : 4-*di*-p-*methoxyphenylbutanoic lactone*, needles (from ethanol) (90%), m. p. 136—137° (Found: C, 73·2; H, 6·2. C$_{18}$H$_{18}$O$_4$ requires C, 72·4; H, 6·0%).

*Reduction of Methyl* 4-*Oxo*-2 : 4-*diphenylbutanoates to Diols*.—Methyl 4-oxo-2 : 4-diphenylbutanoate (5 g.) was extracted from the thimble of a Soxhlet apparatus into ethereal lithium aluminium hydride (1·5 g. in 150 ml. of ether). The mixture was refluxed for a further 2 hr., then excess of hydride was destroyed by the addition of ethyl acetate. 2N-Sulphuric acid (100 ml.) was added, and the ether layer washed with water and evaporated. The resulting syrup solidified under light petroleum (b. p. 40—60°) at 0° in 7 days and 1 : 3-*diphenylbutane*-1 : 4-*diol* (3 g., 66%) was obtained as plates, m. p. 92° (Found: C, 78·9; H, 7·6. C$_{16}$H$_{18}$O$_2$ requires C, 79·3; H, 7·5%). By this method were prepared:

1-p-*Methoxyphenyl*-3-*phenyl*-, cubes (33%), m. p. 48—50° (Found: C, 75·1; H, 7·6. C$_{17}$H$_{20}$O$_3$ requires C, 75·0; H, 7·4%), 1 : 3-*di*-p-*methoxyphenyl*-, needles (81%), m. p. 80—90°

[11] Bergmann, *J. Amer. Chem. Soc.*, 1942, **64**, 557.

(Found: C, 71·2; H, 7·1. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3%), and 3-p-*hydroxyphenyl*-1-*phenylbutane*-1 : 4-*diol*, a gum (Found: C, 73·9; H, 6·8. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%).

*Preparation of Tetrahydro-oxopyridazines.*—Methyl 4-oxo-2 : 4-diphenylbutanoate (20 g.) and phenylhydrazine (6·6 g.) in acetic acid (170 ml.) were heated on a steam-bath for 15 min. The solution was then cooled, diluted with water (100 ml.), and filtered. Recrystallisation of the crystalline residue from ethanol gave 1 : 4 : 5 : 6-tetrahydro-6-oxo-1 : 3 : 5-triphenylpyridazine as plates (18 g., 75%), m. p. 121—123°; Hann and Lapworth [3] gave m. p. 123°. By the same method, or by the use of the acid in place of the methyl ester, were prepared 1 : 4 : 5 : 6-*tetrahydro*-3-p-*methoxyphenyl*-6-*oxo*-1 : 5-*diphenylpyridazine*, plates (85%), m. p. 94—95° (Found: C, 77·2; H, 5·4; N, 7·7. $C_{23}H_{20}O_2N_2$ requires C, 77·5; H, 5·6; N, 7·9%), and 1 : 4 : 5 : 6-*tetrahydro*-3 : 5-*di*-p-*methoxyphenyl*-5-*oxo*-1-*phenylpyridazine*, needles (56%), m. p. 123° (Found: C, 74·6; H, 5·7; N, 7·3. $C_{24}H_{22}O_3N_2$ requires C, 74·6; H, 5·7; N, 7·3%).

*Infrared Spectra.*—4-Hydroxy-2 : 4-di-*p*-methoxyphenylbutenoic lactones had bands as follows: m. p. 106°, 1750 (C:O in 5-membered lactone), 1591 (Ph, conjugated), 1612 and 1514 (aromatic); m. p. 260°, 1763 (C:O in 5-membered lactone), 1579 (Ph, conjugated), 1615 and 1514 cm.$^{-1}$ (aromatic).

We are grateful to Miss E. M. Tanner, Parke Davis & Co., Hounslow, Middlesex, for determinations of the infrared spectra and for suggestions on their interpretation.

THE POLYTECHNIC, 309 REGENT ST., LONDON, W.1. [*Received, November 6th*, 1957.]

---

## 243. *Gibberellic Acid. Part V.* The Relation between Gibberellin $A_1$ and Gibberellic Acid.*

By JOHN FREDERICK GROVE, P. W. JEFFS, and T. P. C. MULHOLLAND.

Gibberellin $A_1$ is a dihydro-derivative of gibberellic acid since one of two dihydro-derivatives obtained by controlled hydrogenation of methyl gibberellate is shown to be identical with gibberellin $A_1$ methyl ester. The isolation of some additional metabolites of *Gibberella fujikuroi* is described.

THE fungus *Gibberella fujikuroi* has been reported to produce several monobasic acidic compounds which promote plant growth. Gibberellic acid,[1] $C_{19}H_{22}O_6$, m. p. 233—235° (decomp.), $[\alpha]_D$ +92°, is produced by several strains (and in particularly high yield by Akers Laboratories no. 917) on the medium described by Borrow *et al.*[2] Working with strains different from the above and using a medium with a higher nitrogen : carbon ratio Takahashi *et al.*[3] obtained a mixture, gibberellin A, from which gibberellin $A_1$, $C_{19}H_{24}O_6$, m. p. 255—258° (decomp.), $[\alpha]_D$ +36°,† and gibberellin $A_2$, $C_{19}H_{26}O_6$,‡ m. p. 235—237° $[\alpha]_D$ +11·7°, were isolated. Using the high-nitrogen medium of the Japanese workers but a different strain of *G. fujikuroi* (N.R.R.L. 2284), Stodola *et al.*[5] obtained a mixture, separated by chromatography on Celite [6] into gibberellin $A_1$ § and gibberellic acid. Gibberellic acid, gibberellin $A_1$, and gibberellin $A_2$ contain respectively two, one, and no ethylenic double bond and differ only in their hydrogen content. The possibility arises therefore that gibberellins $A_1$ and $A_2$ may be reduction products of gibberellic acid. This was also considered by Kitamura *et al.*[4] but their evidence is inconclusive. We have now

* Part IV, *Chem. and Ind.*, 1956, 954.

† Takahashi *et al.* gave m. p. 232—235°, $[\alpha]_D$ +42·3°, but these constants require correction.

‡ Takahashi *et al.* gave $C_{19}H_{28}O_6$, subsequently altered [4] to $C_{19}H_{26}O_6$.

§ The name gibberellin A used [5, 6] for this component of Northern Regional Research Laboratories (N.R.R.L.) gibberellin is discontinued by agreement with Dr. F. H. Stodola.

[1] Cross, *J.*, 1954, 4670.

[2] Borrow, Brian, Chester, Curtis, Hemming, Henehan, Jefferys, Lloyd, Nixon, Norris, and Radley, *J. Sci. Food Agr.*, 1955, **6**, 340.

[3] Takahashi, Kitamura, Kawarada, Seta, Takai, Tamura, and Sumiki, *Bull. Agric. Chem. Soc. Japan*, 1955, **19**, 267.

[4] Kitamura, Seta, Takahashi, Kawarada, and Sumiki, *ibid.*, 1957, **21**, 71.

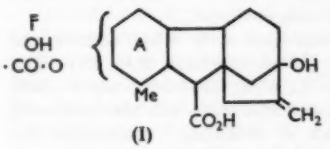
[5] Stodola, Raper, Fennell, Conway, Sohns, Langford, and Jackson, *Arch. Biochem.*, 1955, **54**, 240.

[6] Stodola, Nelson, and Spence, *ibid.*, 1957, **66**, 438.

XUM

shown gibberellin $A_1$ to be a dihydro-derivative of gibberellic acid, but the relation between gibberellic acid and gibberellin $A_2$ requires further investigation.

Separation of the products of the catalytic reduction of gibberellic acid was difficult and better results were obtained with the methyl ester. Hydrogenation of the latter in the presence of a palladium–carbon catalyst resulted in rapid absorption of 1·1—1·2 mol. of hydrogen followed by further slow absorption. Stopping the reaction after absorption of 0·94 mol. of hydrogen gave a mixture from which an acidic and a neutral fraction were isolated. Crystallisation of the latter gave a mixture of methyl dihydrogibberellates, $[\alpha]_D$ +55° (in EtOH), which was resolved with difficulty by chromatography into α- and β-isomers, $[\alpha]_D$ +46° and +74° respectively. The former was identical with gibberellin $A_1$ methyl ester. It follows that gibberellin $A_1$ is a dihydro-derivative of gibberellic acid.



(I)

One of the ethylenic bonds in gibberellic acid is in a terminal methylene group, the other in ring A of the partial structure (I).[7] A terminal methylene group is also present in methyl α-dihydrogibberellate and we have confirmed the production of formaldehyde on ozonolysis reported by Seta *et al.*[8] Methyl α-dihydrogibberellate therefore arises by reduction of the double bond in ring A of methyl gibberellate.

Although Akers Laboratories strain no. 917 produced gibberellic acid and no other gibberellins under the conditions of Borrow *et al.*[2], it gave gibberellin $A_1$ in low yield (and no gibberellic acid) on the high-nitrogen medium of Stodola *et al.*[5] Succinic acid and 5-hydroxymethylfuran-2-carboxylic acid [9] were the only other acidic metabolic products isolated from strain no. 917.

Using the strain and culture conditions described by Stodola *et al.*[5] we have confirmed the production of gibberellin $A_1$ and gibberellic acid. The separation of gibberellin $A_1$ and gibberellic acid on Celite is laborious and separation of the methyl esters by chromatography on alumina is more satisfactory.

Stodola *et al.*[5] also recorded the isolation of fusaric acid, m. p. 106—107°: we have obtained this acid with m. p. 100—101° and also dehydrofusaric acid,[10] m. p. 118—119°, separable by chromatography on Celite. In our view pure fusaric acid has m. p. 100—101°, which is raised by admixture with dehydrofusaric acid, and it seems probable that many of the earlier specimens of fusaric acid [11,12,13] isolated from *G. fujikuroi* contained dehydrofusaric acid. Similar views have been expressed by Gaumann.[14] The infrared spectrum of dehydrofusaric acid showed a strong band at 908 cm.$^{-1}$ absent from the spectrum of fusaric acid: both compounds had bands near 1000 cm.$^{-1}$ but the intensity of a band at 993 cm.$^{-1}$ was greater in dehydrofusaric than in fusaric acid. This evidence suggests the presence of a $\cdot CH{:}CH_2$ group in dehydrofusaric acid, and, taken in conjunction with the ultraviolet absorption of dehydrofusaric acid, which showed the absence of an ethylenic double bond conjugated with the pyridine nucleus, supports the 5-but-3′-enylpyridine-2-carboxylic acid structure for this compound proposed by Stoll and Renz.[15]

## Experimental

M. p.s are corrected. Microanalyses are by Messrs. W. Brown and A. G. Olney. Celite 545 and alumina, Grade II, pH 4 were used in chromatography.

*Separation of Gibberellin $A_1$ and Gibberellic Acid.*—Culture filtrates (200 l.) of *Gibberella*

[7] Cross, Grove, MacMillan, and Mulholland, *Chem. and Ind.*, 1956, 954.
[8] Seta, Kitamura, Takahashi, and Sumiki, *Bull. Agric. Chem. Soc. Japan*, 1957, **21**, 73.
[9] Kawarada, Takahashi, Kitamura, Seta, Takai, and Sumiki, *ibid.*, 1955, **19**, 84.
[10] Stoll, *Phytopath. Z.*, 1954, **22**, 233.
[11] Yabuta, Kambe, and Hayashi, *J. Agric. Chem. Soc. Japan*, 1934, **10**, 1059.
[12] Plattner, Keller, and Boller, *Helv. Chim. Acta*, 1954, **37**, 1379.
[13] Nakashima, *J. Pharm. Soc. Japan*, 1955, **75**, 1010.
[14] Gaumann, *Phytopath. Z.*, 1957, **29**, 1.
[15] Stoll and Renz, *ibid.*, p. 380.

*fujikuroi* (*Fusarium monoiliforme*) N.R.R.L. 2284 were extracted by the method of Borrow *et al.*,[2] giving crude gibberellin (2·30 g.), m. p. 235—238° (decomp.), $[\alpha]_D^{20}$ +53° (11·5 mg./l.) and, on evaporation of the ethyl acetate mother-liquor, a gum (*B*) (3·44 g.).

Crude gibberellin (300 mg.) in ether (200 ml.) was run on to a Celite column (53 × 8 cm.) buffered at pH 7·0, and elution continued with ether previously saturated with water. When solid began to appear in the eluate, aliquot parts (200 ml.) were collected.

(*a*) Eluates 1—52 gave a gum (102 mg.) which on trituration with ethyl acetate and recrystallisation of the resulting solid furnished gibberellin $A_1$ (15 mg.), prisms, m. p. 255—258° (decomp.), $[\alpha]_D^{20}$ +38° ± 3 (*c* 0·39 in EtOH), p*K* 4·3 (Found: C, 65·3; H, 6·9%; equiv., 354. Calc. for $C_{19}H_{24}O_6$: C, 65·5; H, 6·9%; *M*, 348). The infrared spectrum was identical with that of gibberellin $A_1$[3] and with the spectrum of a specimen of N.R.R.L. " gibberellin A," m. p. 258° (decomp.), $[\alpha]_D^{20}$ +36·5° (*c* 0·4 in EtOH), supplied by Dr. F. H. Stodola.

The m. p. of gibberellic acid was raised on admixture with gibberellin $A_1$. Gibberellin $A_1$ did not give the characteristic red colour and blue fluorescence in concentrated sulphuric acid given by gibberellic acid; it gave a straw yellow solution which slowly developed a weak greenish fluorescence during several days. $R_F$ values (Whatman No. 1 paper; descending chromatograms) for gibberellin $A_1$ run in 4 : 5 : 1 butanol–water–ammonia solution (*d* 0·88) (bromocresol-green spray) and in 20 : 4 : 2 : 1 chloroform–ethanol–water–formic acid (19 : 1 ethanol–sulphuric acid spray) were identical with those found for gibberellic acid, *viz.*, 0·31 and 0·80 respectively. The fluorescent spot developed by spraying with ethanolic sulphuric acid was very much less intense than that produced by gibberellic acid.

The methyl ester, prepared in methanol with ethereal diazomethane, formed needles, m. p. 234—235° [from ethyl acetate–light petroleum (b. p. 60—80°)], $[\alpha]_D^{20}$ +46° (*c* 0·41 in EtOH), +36·5° (*c* 0·41 in acetone) (Found: C, 66·4; H, 7·4. Calc. for $C_{20}H_{26}O_6$: C, 66·3; H, 7·2%). The infrared spectrum was identical with those of gibberellin $A_1$ methyl ester [3] and of the methyl ester prepared from N.R.R.L. " gibberellin A."

(*b*) Eluates 53—74 gave a gum (54 mg.), $[\alpha]_D$ +58°, which was a mixture of gibberellin $A_1$ and gibberellic acid.

(*c*) Eluates 75—154 gave a solid (145 mg.) which on crystallisation from ethyl acetate–light petroleum (b. p. 60—80°) furnished gibberellic acid (134 mg.), m. p. 232—235° (decomp.), $[\alpha]_D$ +90°, identified by its infrared spectrum.

It is not claimed that the above method of separation, worked out independently of that of Stodola *et al.*,[6] has any advantages over the latter: indeed, the recovery of gibberellin $A_1$ is lower than that achieved by the N.R.R.L. workers.

The gum (*B*) was chromatographed in ether (250 ml.) on Celite (45 × 3 cm.; pH 7·0). Elution was effected with ether (500 ml. portions). All eluates were free from gibberellin $A_1$ and gibberellic acid, as shown by the absence of an absorption band at 1784 $cm.^{-1}$ (lactone C=O) in dioxan solution.

Eluate 3 gave material (845 mg.) which on crystallisation from ethyl acetate yielded fusaric acid (102 mg.), m. p. 95—98°, purified by sulimation at 90°/$10^{-4}$ mm. and further crystallisation from ethyl acetate. It formed prisms, m. p. 100—101° (Found: C, 66·7; H, 7·3. Calc. for $C_{10}H_{13}O_2N$: C, 67·0; H, 7·3%), identical (mixed m. p. and infrared spectrum) with an authentic specimen. The m. p. of fusaric acid was raised on admixture with dehydrofusaric acid (see below).

Material (659 mg.) from eluates 5—18, on crystallisation from ethyl acetate, sublimation at 80—100°/$10^{-4}$ mm., and two recrystallisations from ethyl acetate, furnished dehydrofusaric acid (243 mg.), prismatic needles, m. p. 118—119° (Found: C, 67·6; H, 6·8; N, 8·1%; equiv., 167. Calc. for $C_{10}H_{11}O_2N$: C, 67·8; H, 6·3; N, 7·9%; *M*, 177), $\lambda_{max.}$ (in EtOH) 230, 270 mμ (log ε 4·00, 3·71), identical (mixed m. p. and infrared spectrum) with an authentic specimen kindly provided by Dr. C. Stoll, E.T.H., Zurich.

Material (421 mg.) from eluate 4 furnished prisms (136 mg.) (from ethyl acetate), m. p. 104—105°, shown by the infrared spectrum to be a mixture of fusaric and dehydrofusaric acid.

*Separation of Gibberellin $A_1$ Methyl Ester and Methyl Gibberellate.*—Crude gibberellin, $[\alpha]_D^{20}$ +53° (385 mg.), from strain N.R.R.L. 2284, in methanol (10 ml.) was treated with ethereal diazomethane in ether. After 24 hr. the excess of diazomethane and solvents were removed and the residual gum (400 mg.) was chromatographed in 200 : 1 benzene–methanol (75 ml.) on alumina (15·5 × 2 cm.), fractional elution (50 ml. eluates) being used. Eluates 8—14 [benzene–methanol (200 : 1)], yielded gibberellin $A_1$ methyl ester (157 mg.), m. p. 225—232°. Eluates

15—17 [benzene–methanol (200 : 1)] and 18—21 [benzene–methanol (50 : 1)] yielded methyl gibberellate (150 mg.), m. p. 200—203°. Both products were identified by their infrared spectra.

In our hands the method of Takahashi *et al.*[3] using ethyl acetate–benzene as eluant was less successful.

*Investigation of the Metabolic Products of* G. fujikuroi *strain* 917.—(a) *Cultured on the medium of Borrow* et al.[2] In the standard procedure [16] for isolating gibberellic acid the final ethyl acetate extract is concentrated until crystals of gibberellic acid begin to appear and when crystallisation is complete the gibberellic acid is filtered off; for this experiment one-tenth of the final ethyl acetate extract of the culture filtrate (5 l.) was evaporated completely *in vacuo* at 20°, giving a sticky solid (85 mg.), $[\alpha]_D$ +52°. This was chromatographed in ether (100 ml.) on Celite (25 × 1·5 cm.; pH 7), elution being with 100 ml. portions of ether. Material from eluates 3—8 had $[\alpha]_D^{22}$ +88°, m. p. 233—238° (decomp.) (15 mg.) and consisted of gibberellic acid (30 mg./l.). Material (20 mg.) from eluates 9—12 deposited prisms, m. p. 175—180°, of succinic acid on crystallisation from ethyl acetate–light petroleum (b. p. 60—80°).

(b) *Cultured on the medium of Stodola* et al.[5] After extraction of the culture filtrate (67 l.) by the method of Borrow *et al.*[2] the ethyl acetate was removed *in vacuo*, furnishing a gum (101 mg.). This was chromatographed in ether (100 ml.) on Celite as described above. Material (27 mg.), $[\alpha]_D^{20}$ +49°, from eluates 3—5 yielded gibberellin $A_1$ (4 mg.; 0·06 mg./l) as prisms, m. p. 233—237° (decomp.), identified by the infrared spectrum. Material (18 mg.) from eluates 9—13 gave succinic acid (2 mg.).

A result almost identical with this was obtained by using the methanolic ammonia extraction procedure of Stodola *et al.*[5]

(c) *Isolation of 5-hydroxymethylfuran-2-carboxylic acid.* On one occasion the crude gibberellic acid from strain no. 917 had an abnormally low m. p. of 155—175° (decomp.). The crude material (10 g.) was heated under reflux with ethyl acetate (900 ml.; charcoal) and, after filtration, boiling light petroleum (b. p. 60—80°; 1 l.) was added. After 2 hr. at room temperature and 24 hr. at 0° the crystalline material was removed, giving gibberellic acid (3·80 g.), m. p. 218—220° (decomp.), $[\alpha]_D^{17}$ +82°. Concentration of the mother-liquors afforded crude 5-hydroxymethylfuran-2-carboxylic acid (4·40 g.), m. p. 155—160° (decomp.), purified by further crystallisation from ethyl acetate. It formed prisms, m. p. 163—165° (decomp.), p*K* 3·5 (Found: C, 50·9; H, 4·6%; equiv., 143. Calc. for $C_6H_6O_4$: C, 50·7; H, 4·3%; *M*, 142), $\lambda_{max.}$ (in EtOH) 258 mμ (log ε 4·13), identical (mixed m. p. and infrared spectrum) with a specimen provided by Dr. H. W. B. Reed, Imperial Chemical Industries Limited, Billingham Division.

*Hydrogenation of Methyl Gibberellate.*—A solution of methyl gibberellate (3·30 g.) in ethyl acetate (180 ml.) was shaken with 10% palladium–carbon (1·0 g.; prepared from nitric acid-washed carbon [17]) in hydrogen at 19°. When 0·94 mol. of hydrogen had been absorbed (21 min.) the catalyst was filtered off and the filtrate was extracted with sodium carbonate, washed with water, dried ($Na_2SO_4$), and evaporated, giving a neutral solid (1·83 g.).

The acidified alkaline extract was re-extracted with ethyl acetate, giving on recovery a semicrystalline acidic product (0·68 g.) which will be discussed in a later paper.

The combined neutral products (3·74 g.) from two experiments were fractionally crystallised from ethyl acetate. Fractions with m. p. between 225° and 234° (decomp.) (3·10 g.), $[\alpha]_D^{20}$ +55° ± 3°, were chromatographed in benzene (1·5 l.) on alumina (30 × 5·0 cm.). Elution with 200 : 1 benzene–methanol (500 ml. aliquot parts) gave, after a forerun, (1) 0·35 g., (2) 0·41 g., (3) 0·37 g., (4)—(14), 1·62 g. Further elution with 100 : 1 benzene–methanol gave (15)—(19) 0·15 g.

Recrystallisation of fractions (1) and (2) from ethyl acetate–light petroleum gave *methyl α-dihydrogibberellate* as needles, m. p. 233—235° (decomp.), $[\alpha]_D^{24}$ +46° ± 3° (*c* 1·04 in EtOH), $[\alpha]_D^{24}$ +31° ± 3° (*c* 0·93 in acetone) (Found: C, 66·6, 66·3; H, 7·4, 7·5. $C_{20}H_{26}O_6$ requires C, 66·3; H, 7·2%). In acetic acid in the presence of palladium black it took up 0·7 mol. of hydrogen.

The infrared absorption spectrum was identical with that of gibberellin $A_1$ methyl ester prepared (as above) by methylation of gibberellin $A_1$ obtained from *G. fujikuroi*. Mixed m. p. determinations showed no depression.

[16] Curtis and Cross, *Chem. and Ind.*, 1954, 1066.
[17] Vogel, " Practical Organic Chemistry," Longmans, Green and Co., London, 1948, p. 989.

XUM

Fraction (3), $[\alpha]_D$ +46°, contained traces (infrared spectrum) of the β-isomer (see below) which was present in increasing amounts in fractions (4)—(14).

Fractions (15)—(19) crystallised from ethyl acetate–light petroleum in needles of *methyl β-dihydrogibberellate*, m. p. 227—230° (decomp.), $[\alpha]_D^{17}$ +74° (*c* 1·02 in EtOH) (Found: C, 66·2; H, 7·3%). Microhydrogenation showed 0·9 ethylenic bond.

*Ozonolysis of Methyl α-Dihydrogibberellate.*—Ozonised oxygen (100 ml./min., 4·8 mg. of $O_3$/min.) was passed into a solution of the ester (107 mg.) in acetic acid (10 ml.) at 20° until absorption ceased (10 min.). The solution was diluted with water (10 ml.) and steam-distilled. The distillate was treated with an equal volume of saturated dimedone solution and set aside for 48 hr. Needles, m. p. 182—185° (53·4 mg., 0·6 mol.), of the dimedone derivative of formaldehyde separated from the first 100 ml. of distillate. Recrystallisation from 50% ethanol gave needles (46·2 mg.), m. p. 188—189°, identical (mixed m. p. and infrared spectrum) with an authentic specimen. The non-steam-volatile products will be discussed in a later paper.

We are indebted to Dr. H. W. B. Reed, Dr. F. H. Stodola, and Dr. C. Stoll for specimens, to Dr. L. A. Duncanson and Mr. M. B. Lloyd for infrared spectra, to Mr. I. S. Nixon for carrying out the fermentations, and to Messrs. S. C. Bishop, D. Gardner, and P. H. Melvin for technical assistance.

AKERS RESEARCH LABORATORIES, IMPERIAL CHEMICAL INDUSTRIES LIMITED,
THE FRYTHE, WELWYN, HERTS. [*Received, November 11th*, 1957.]

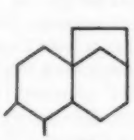
---

## 244. *Synthesis of Some Angularly Bridged Cyclic Systems. Part I. Perhydrobenz*[d]*indole.*

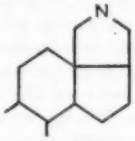
By R. D. HAWORTH and A. F. TURNER.

1-Oxo-*cis*-9-decalylacetic acid (X; R = H) has been prepared from 2-*N*-methylanilinomethylene-1-decalone and ethyl bromoacetate, and converted into perhydrobenz[*d*]indole (III; R = H). The configuration of the acid (X; R = H) has been established by descent and reduction to *cis*-decalin-9-carboxylic acid, identical with a specimen obtained by a second and unambiguous synthesis.

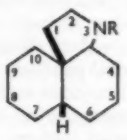
RESEARCHES in progress in these laboratories on cafestol and conessine [1] have emphasised the importance of angular homo- and hetero-cyclic systems (I) and (II) respectively and led to a number of investigations aiming at the synthesis of these and similar ring systems. The present communication describes experiments, based on 1-decalone as starting material, which have culminated in the synthesis of the base (III).



(I)




(II)

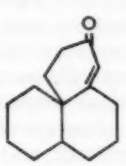


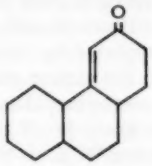

(III)

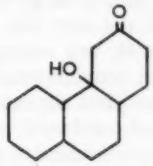
As α-alkylated ketones are reported [2,3,4] to react with methyl vinyl ketones at the methine rather than the methylene carbon atom, it was expected that 1-decalone would yield the angular system (IV) instead of the isomeric phenanthrene type. However, no success attended attempts to bring about reaction between 1-decalone and 4-diethylaminobutan-2-one methiodide under conditions which have met with success in other fields.[2,3,5] Experiments with 2-*iso*propoxymethylene-1-decalone were equally unsuccessful

[1] Haworth and Johnstone, *J.*, 1957, 1492; Haworth and Michael, *J.*, 1957, 4973.
[2] du Feu, McQuillin, and Robinson, *J.*, 1937, 53.
[3] Robinson and Weygand, *J.*, 1941, 386.
[4] Cornforth and Robinson, *J.*, 1946, 676.
[5] Ghosh and Robinson, *J.*, 1944, 506.

and, when pyridine was used as solvent,[6] condensation occurred and the dodecahydro-3-oxophenanthrene (V) and perhydro-12-hydroxy-3-oxophenanthrene (VI) were isolated, but we are unable to give a satisfactory explanation of the removal of the enol ether group. The structures of these two products were in agreement with spectroscopic data; the ketol (VI) displayed infrared maxima at 3252 and 1715 cm.$^{-1}$ (hydroxy and keto-group


(IV)

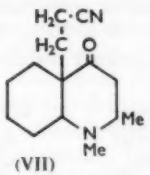

(V)



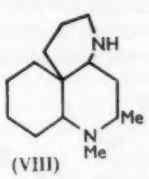
(VI)

respectively [7]), and the αβ-unsaturated ketone (V) showed an ultraviolet absorption maximum at 240 mμ, consistent [8,9] with the ββ-disubstitution and an exocyclic double bond. The ketol (VI) was smoothly dehydrated by ethanolic hydrochloric acid to compound (V), and the latter, after conversion by Huang-Minlon [10] reduction [10] into 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9 : 10 : 11 : 13 : 14-dodecahydrophenanthrene (not purified), was dehydrogenated with selenium in excellent yield to phenanthrene. The ketone (V) and ketol (VI) were also prepared from 2-formyl-1-decalone, condensation in this case being directed to the 2-position by the known [11,12] activating influence of the formyl group.

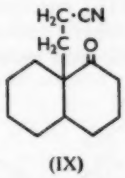
Recently Nazarov *et al.*[13] have described the cyanoethylation of perhydro-1 : 2-dimethyl-4-quinolone to 10-2′-cyanoethylperhydro-1 : 2-dimethyl-4-quinolone (VII), and shown that reductive cyclisation of this product yielded the diacidic base (VIII). 1-Decalone reacted similarly with acrylonitrile in the presence of potassium hydroxide, to give an oil containing the cyanoethyl derivative (IX). The infrared maxima at 2255 and 1695 cm.$^{-1}$ were assigned to the aliphatic nitrile [7] and the keto-group respectively, and the oil gave a crystalline 2 : 4-dinitrophenylhydrazone. The oil also yielded a crystalline 2-piperonylidene derivative with infrared maxima at 2263 (C≡N group [7]) and 1664 cm.$^{-1}$ (conjugated C=O group), and the isolation of this derivative provided evidence of the presence of the 9-cyanoethyl derivative (IX). Hydrolysis of the crude cyano-



(VII)



(VIII)



(IX)

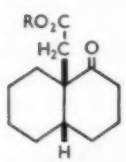
ethylation product, however, gave an inseparable mixture of acids; on one occasion a pure β-(1-oxodecalyl)propionic acid was obtained but the experiment could not be repeated, and it was not possible to determine whether this specimen was derived from the nitrile (IX) or from the isomeric nitrile with the cyanoethyl group in position 2.

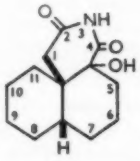
The most fruitful approach discovered during these experiments with 1-decalone is based upon the introduction of an acetic acid residue into position 9. 2-*N*-Methylanilinomethylene-1-decalone was condensed with ethyl bromoacetate in presence of sodamide

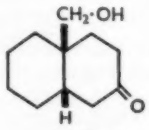
[6] McQuillin, *J.*, 1955, 528.
[7] Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen, London, 1954.
[8] Woodward, *J. Amer. Chem. Soc.*, 1942, **65**, 76.
[9] Fieser, Fieser, and Rajogopalan, *J. Org. Chem.*, 1948, **13**, 800.
[10] Huang-Minlon, *J. Amer. Chem. Soc.*, 1949, **71**, 3301.
[11] Wilds and Werth, *J. Org. Chem.*, 1952, **17**, 1149; 1952, **17**, 1154.
[12] Wilds and Schunk, *J. Amer. Chem. Soc.*, 1949, **71**, 3946; 1950, **72**, 2388.
[13] Nazarov, Schuckhgeimer, and Rudenko, *Zhur. obschei Khim.*, 1954, **24**, 319.

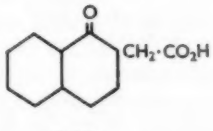
XUM

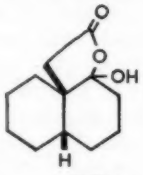
and, after the two-stage hydrolytic procedure [14] for removal of the blocking group, 1-oxo-*cis*-9-decalylacetic acid (X; R = H) was obtained. This keto-acid gave a crystalline oxime and 2 : 4-dinitrophenylhydrazone; attempted conversion into the cyanohydrin gave a compound insoluble in sodium hydrogen carbonate but soluble in sodium hydroxide solution, and its probable imide structure (XI) was supported by the infrared maxima at 3355 (OH group), 3187 (NH group), 1730 and 1694 cm.$^{-1}$ (imide-CO group). Attempted decarboxylation of the acid (X; R = H) to 9-methyl-1-decalone was unsuccessful but structure (X; R = H) was strongly supported by Clemmensen reduction to *cis*-9-decalylacetic acid which on dehydrogenation in the vapour phase over palladium–charcoal [15] gave naphthalene in poor yield instead of 2-methylnaphthalene which would be expected from the isomeric *cis*-2-decalylacetic acid. Final proof of the structure (X; R = H) was obtained by Barbier–Wieland degradation [16] of *cis*-9-decalylacetic acid to *cis*-decalyl-9-carboxylic acid, which differed from the known *trans*-isomer [17] but was identical with a specimen of *cis*-decalin-9-carboxylic acid prepared from 10-hydroxymethyl-*cis*-2-decalone


(X)


(XI)

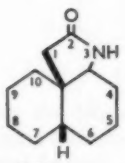

(XII)

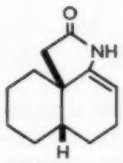

(XIII)

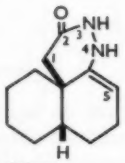

(XIV)

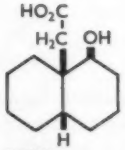
(XII). The *cis*-structure of (XII) has been established by Minckler, Hussey, and Baker,[18] and Clemmensen reduction followed by oxidation with chromic acid gave *cis*-decalin-9-carboxylic acid. (This acid has also been described by Dauben and Rogan [19] after this communication had been prepared.) 1-Oxo-2-decalylacetic acid (XIII) was also synthesised, for comparison, from 2-formyl-1-decalone and ethyl bromoacetate. A peculiar result was obtained during an attempted preparation of the homologue of acid (X; R = H); the sodium salt, on treatment with oxalyl chloride followed by diazomethane, gave a substance, $C_{12}H_{18}O_3$, m. p. 67—69°, which contained neither nitrogen nor chlorine, and was reconverted into 1-oxo-*cis*-9-decalylacetic acid on hydrolysis. The lactone structure (XIV) has been considered but requires confirmation.

When methyl or ethyl 1-oxo-*cis*-9-decalylacetate (X; R = Me or Et) was treated with formamide and formic acid under conditions of the Leuckart reaction, the lactam (XV)


(XV)


(XVI)


(XVII)


(XVIII)

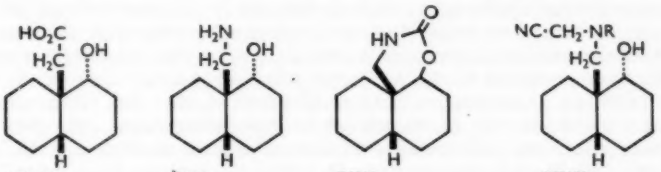
was obtained. The structure (XV) was supported by the infrared maxima at 3219 and 3053 (NH group) and 1694 cm.$^{-1}$ ($\gamma$-lactam CO group).[7] When treated with lithium aluminium hydride, the lactam (XV) was converted into the oily secondary base (III;

[14] Birch and Robinson, *J.*, 1944, 501.
[15] Linstead and Thomas, *J.*, 1940, 1127.
[16] Barbier and Locquin, *Compt. rend.*, 1913, 156, 1443; Wieland, Schlichting, and Jacobi, *Z. physiol. Chem.*, 1926, **161**, 80.
[17] Dauben, Tweit, and MacLean, *J. Amer. Chem. Soc.*, 1955, **77**, 48; Hussey, Liao, and Baker, *ibid.*, 1953, **25**, 4727.
[18] Minckler, Hussey, and Baker, *ibid.*, 1956, **78**, 1009.
[19] Dauben and Rogan, *ibid.*, 1957, **79**, 5002.

R = H), characterised as the hydrobromide and methylated by formaldehyde and formic acid to the oily tertiary base (III; R = Me) which gave a crystalline methiodide.

Methyl 1-oxo-*cis*-9-decalylacetate (X; R = Me) reacted with methanolic ammonia but the amide could not be purified because of its ready conversion into the unsaturated lactam (XVI), which was reduced catalytically to (XV). Similarly methyl 1-oxo-*cis*-9-decalylacetate (X; R = Me) with hydrazine yielded the cyclic hydrazide (XVII) which furnished an *N*-nitroso-derivative; this hydrazide was also obtained by the action of hydrazine on the oxime of methyl 1-oxo-*cis*-9-decalylacetate, but attempts to reduce it to the perhydro-derivative were unsuccessful.

1-Oxo-*cis*-9-decalylacetic acid (X; R = H) was reduced with sodium borohydride, to a mixture of a hydroxy-acid, m. p. 118°, which gave an oily lactone, and a γ-lactone (CO maximum at 1780 cm.$^{-1}$), m. p. 66°. The hydroxy-acid corresponding to the γ-lactone, m. p. 66°, could not be isolated although hydrolysis of the oily lactone readily gave the hydroxy-acid, m. p. 118°. The two isomeric 2-hydroxy*cyclo*hexylacetic acids show a similar behaviour and Newman and VanderWerff [20] have assigned a *cis*-structure to the lactone from which the corresponding hydroxy-acid could not be isolated. On this basis the γ-lactone of m. p. 66° is the lactone of *cis*-1-hydroxy-*cis*-9-decalylacetic acid * (XVIII),




(XIX) (XX) (XXI) (XXII)

and the acid of m. p. 118° is *trans*-1-hydroxy-*cis*-9-decalylacetic acid (XIX). *trans*-1-Hydroxy-*cis*-9-decalylacetic acid (XIX) was also prepared from the keto-acid (X; R = H) either by catalytic reduction or by alkoxide reduction of the methyl ester. The observation that *both* stereoisomers (XVIII) and (XIX) may be lactonised provides further evidence for the *cis*-fusion of the rings, as, if chair conformation of the rings is assumed, a *trans*-1-hydroxy-*trans*-9-decalylacetic acid must have a diaxial conformation of both substituents and lactonisation would be impossible.

An attempt to convert *trans*-1-oxo-*cis*-9-decalylacetic acid (XIX) into *trans*-9-aminomethyl-*cis*-1-decalol (XX) *via* the hydrazide gave the cyclic urethane (XXI) in poor yield. However the amide of the acid (XIX), prepared from the methyl ester by methanolic ammonia, was successfully degraded to the base (XX) by the Hofmann procedure. Attempts to oxidise *trans*-9-aminomethyl-*cis*-1-decalol (XX) to the corresponding 1-decalone were unsuccessful, but it was converted into *trans*-9-(*N*-cyanomethylaminomethyl)-*cis*-1-decalol (XXII; R = H) by the action of formaldehyde and potassium cyanide. This oily base (XXII; R = H), which gave a crystalline hydrochloride, was methylated to *trans*-9-(*N*-cyanomethyl-*N*-methylaminomethyl)-*cis*-1-decalol (XXII; R = Me), characterised as the methiodide, but again oxidation to the decalone could not be effected.

## Experimental

Light petroleum refers to the fraction of b. p. 40—60°, ligroin refers to the fraction of b. p. 60—80°, and N-aqueous-methanolic potassium hydroxide refers to a solution prepared by dissolving potassium hydroxide (5·65 g.) in water (5 c.c.) and adding methanol to bring the

* Following Minckler *et al.*,[8] the relationship of the angular and peripheral substituents prefixes the name and the nature of the ring fusion is expressed as a prefix to the root of the name. The reference group is the 9-substituent.

[20] Newman and VanderWerff, *J. Amer. Chem. Soc.*, 1945, **67**, 233.

volume to 100 c.c. 1-Decalol, prepared by Birch and Robinson's method [14] using W-7 Raney nickel, was oxidised to 1-decalone as described by Johnson and Posvic.[21]

*Perhydro-12-hydroxy-3-oxophenanthrene* (VI) *and* 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9 : 10 : 11 : 13 : 14-*Dodecahydro-3-oxophenanthrene* (V).—(a) *From* 2-*iso*propoxymethylene-1-*decalone*. A solution of 2-*iso*propoxymethylene-1-decalone [21] (7·3 g.) in ether (150 c.c.) was heated in dry nitrogen with potassamide prepared from potassium (1·41 g.) and liquid ammonia (30 c.c.) with ferric nitrate (20 mg.) as catalyst. A solution of the methiodide (9·4 g.) of 4-diethylaminobutan-2-one [22] in pyridine (50 c.c.) was added rapidly and with stirring to the deep red suspension at 0°, and the mixture, after 8 hr. at 0° and 12 hr. at room temperature, was refluxed for 5 hr. After addition of water, the mixture was extracted with ether; removal of the solvent gave a thick red oil (4·3 g.), which, after being freed from pyridine at 100°/0·1 mm. (2 hr.), was treated with ferric chloride (15 g.) in methanol (40 c.c.) for 2 hr. at 0°. The product, isolated with ether and washed successively with dilute hydrochloric acid and sodium hydroxide, was a neutral brown oil (3·6 g.).

(b) *From* 2-*formyl*-1-*decalone*. To a solution of sodium (4·20 g.) in methanol (30 c.c.) was added 2-formyl-1-decalone [21] (3·00 g.) in methanol (10 c.c.), followed by the methiodide (8·8 g.) of 4-diethylaminobutan-2-one in pyridine (20 c.c.). After 4 days, water was added and the neutral product isolated with ether as a brown oil (3·6 g.).

Chromatography of the products from either (a) or (b) on alumina (100 g.) gave (i), by light petroleum, an oil (0·10 g.), (ii) by light petroleum–benzene (1 : 1), an oil (0·23 g.), (iii) by benzene, an oil (0·48 g.), (iv) by benzene–ether (1 : 1), an oil (0·12 g.), (v) by ether, oily crystals (0·35 g.), (vi) by ether–chloroform (1 : 1), oily crystals (0·65 g.), (vii) by chloroform, oily crystals (0·35 g.), (viii) by chloroform–methanol (1 : 1), a viscous yellow oil (0·75 g.), and (ix) by methanol, a brown tar (0·25 g.). Combination and distillation of the first three fractions gave 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9 : 10 : 11 : 13 : 14-*dodecahydro-3-oxophenanthrene* (V) (0·69 g.), b. p. 120—130° (bath)/0·001 mm., which slowly crystallised as stout needles, m. p. 53—54° (Found: C, 82·0; H, 10·1. $C_{14}H_{20}O$ requires C, 82·3; H, 9·9%), $\lambda_{max.}$ 240 mμ (log ε 4·2 in EtOH). The *semicarbazone* separated from methanol in plates, m. p. 225—226° (Found: C, 69·4; H, 8·6; N, 16·3. $C_{15}H_{23}ON_3$ requires C, 68·9; H, 8·9; N, 16·1%). Fractions (v), (vi), and (vii), combined and crystallised first from light petroleum and then from ligroin, gave *perhydro-12-hydroxy-3-oxophenanthrene* (VI) (0·7 g.) as needles, m. p. 128—129° (Found: C, 75·8; H, 9·9. $C_{14}H_{22}O_2$ requires C, 75·7; H, 9·9%). The infrared spectrum (KBr disc) showed absorption at 1715 and 3525 cm.$^{-1}$. Dehydration of the ketol (VI) (200 mg.) with concentrated hydrochloric acid (0·3 c.c.) in ethanol (3 c.c.) took place at room temperature and yielded the dodecahydro-3-oxophenanthrene (170 mg.) (V), m. p. 53—54°.

*Conversion of the Ketone* (V) *into Phenanthrene*.—The unsaturated ketone (V) (300 mg.) was refluxed for 0·5 hr. with hydrazine hydrate (290 mg.) in diethylene glycol (20 c.c.). Potassium hydroxide (270 mg.) in a little water was added, the mixture was refluxed for another 0·5 hr., concentrated until the temperature of the liquid was 200°, and finally refluxed for 2 hr. 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9 : 10 : 11 : 13 : 14-Dodecahydrophenanthrene, isolated with ether as an oil (183 mg.), b. p. (bath) 180°/10 cm., was heated with selenium (600 mg.) at 320° for 12 hr.; phenanthrene (160 mg.), m. p. 93—94° (picrate, m. p. 143—144°), was obtained.

9-2′-*Cyanoethyl*-1-*decalone* (IX).—A mixture of 1-decalone (15·7 g.), acrylonitrile (1·88 g.), and 40% potassium hydroxide solution (0·9 c.c.) was stirred for 24 hr. and then set aside for 3 days. Excess of hydrochloric acid was added and the product, isolated with ether, was an oil from which unchanged 1-decalone (13·0 g.) was recovered by distillation. The residue was adsorbed on an alumina (30 g.) column and eluted first with ether–light petroleum (1 : 20) and then with ether. Evaporation of the ether yielded crude 9-2′-cyanoethyl-1-decalone (IX) (1·79 g.), b. p. 120°/0·5 cm.; the infrared spectrum (Nujol mull) showed maxima at 2255 and 1695 cm.$^{-1}$. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol in orange needles, m. p. 180° (Found: C, 59·1; H, 6·2; N, 17·9. $C_{19}H_{23}O_4N_5$ requires C, 59·2; H, 6·0; N, 18·2%).

9-2′-*Cyanoethyl*-2-*piperonylidene*-1-*decalone*, prepared from 9-2′-cyanoethyl-1-decalone (97 mg.), piperonaldehyde (81 mg.), and 15% sodium hydroxide solution (0·18 c.c.), crystallised from ethanol in yellow plates, m. p. 127° (Found: C, 74·3; H, 7·1; N, 4·0. $C_{21}H_{23}O_3N$ requires C, 74·7; H, 6·9; N, 4·1%). The infrared spectrum (KBr disc) showed maxima at 2263 and 1664 cm.$^{-1}$. Crude 9-2′-cyanoethyl-1-decalone (IX), when hydrolysed for 12 hr. with excess

[21] Johnson and Posvic, *ibid.*, 1947, **69**, 1361.
[22] Wilds and Schunk, *J. Amer. Chem. Soc.*, 1943, **65**, 469; Cornforth and Robinson, *J.*, 1949, 1855.

of boiling 30% sodium hydroxide solution, usually gave an *acid* mixture which after several crystallisations from ligroin had m. p. 78—90°; on one occasion needles, m. p. 130° (Found: C, 69·3; H, 9·1. $C_{12}H_{20}O_3$ requires C, 69·6; H, 9·0%), were obtained.

1-*Oxo*-cis-9-*decalylacetic acid* (X; R = H).—A solution of 2-*N*-methylanilinomethylene-1-decalone [14] (50 g.) in benzene (200 c.c.) was added to a stirred suspension of sodamide, prepared in a nitrogen atmosphere by addition of sodium (4·3 g.) to liquid ammonia (100 c.c.) containing ferric nitrate (50 mg.) in benzene (100 c.c.), the whole being then boiled for 4 hr. Ethyl bromoacetate (31 g.) was added to the cooled suspension, and reaction completed by 2 hours' refluxing. The solvent was removed under reduced pressure and the residual gum refluxed for 1 hr. with water (400 c.c.) and concentrated hydrochloric acid (200 c.c.). The top insoluble layer was taken up in ether and, after removal of the solvent, the hydrolysis was completed by 1 hour's boiling with 20% aqueous sodium hydroxide (300 c.c.). Unchanged 1-decalone (13·6 g.) was removed in ether, and the acid (X; R = H) recovered from the alkaline layer was isolated with ether and purified by distillation; it was obtained as a viscous yellow oil, b. p. 150—180°/0·03 mm. with some decomposition, which separated from carbon tetrachloride or ether–ligroin in rods (5·0 g.), m. p. 100° (Found: C, 68·2; H, 8·8. $C_{12}H_{18}O_3$ requires C, 68·5; H, 8·6%). The yield was not improved by the use of potassamide or triphenylmethylsodium as condensing agent. The 2 : 4-*dinitrophenylhydrazone* crystallised from aqueous acetic acid in pale orange needles, m. p. 203—210° (decomp.) (Found: C, 55·4; H, 5·7; N, 14·0. $C_{18}H_{22}O_6N_4$ requires C, 55·4; H, 5·7; N, 14·3%). The *oxime* crystallised from aqueous ethanol in colourless needles, m. p. 166—169° (decomp.) (Found: C, 63·8; H, 8·6; N, 6·0. $C_{12}H_{19}O_3N$ requires C, 64·0; H, 8·5; N, 6·2%). A mixture of hydrogen cyanide (2·3 g.) and sodium cyanide (180 mg.) in the minimum of water was added to a solution of the keto-acid (X; R = H) (210 mg.) in methanol (7·0 c.c.). After 24 hr. the hydrogen cyanide was removed, dilute hydrochloric acid and chloroform were added, and the chloroform extract yielded a pale brown oil (230 mg.) which was refluxed for 0·5 hr. with 2N-sulphuric acid (10 c.c.). The product was taken up in ether, unchanged keto-acid (X; R = H) (64 mg.) was removed by washing with sodium hydrogen carbonate, and the residual neutral *perhydro-4a-hydroxy*-2 : 4-*dioxobenzo*[e]iso-*quinoline* (XI) (113 mg.) separated from benzene in small colourless needles, m. p. 193—194° (Found: C, 65·6; H, 7·9; N, 5·9. $C_{12}H_{19}O_3N$ requires C, 65·8; H, 8·1; N, 5·9%), which dissolved in aqueous sodium hydroxide but not in sodium hydrogen carbonate; the infrared spectrum (KBr disc) showed maxima at 3355, 3187, 1730, and 1694 cm.$^{-1}$. Powdered sodium 1-oxo-9-decalylacetate (856 mg.), prepared from the acid and sodium hydrogen carbonate, was suspended in benzene (15 c.c.) containing pyridine (1 drop), and oxalyl chloride (3·5 c.c.) was added. After 2 hr., the solvents were removed under reduced pressure and the residue was taken up in benzene (15 c.c.) and added to an excess of diazomethane in ether. After another hr. the mixture was washed successively with dilute hydrochloric acid and water, dried, and evaporated. The product, probably the *lactone* (XIV), separated from light petroleum in long needles, m. p. 67—69° (Found: C, 67·8; H, 8·4. $C_{12}H_{18}O_3$ requires C, 68·5; H, 8·6%).

1-*Oxo*-2-*decalylacetic Acid*.—2-Formyl-1-decalone (1·51 g.), dissolved in a little methanol, was added to a solution of sodium methoxide (from sodium, 200 mg.) in methanol (15 c.c.). Ethyl bromoacetate (1·37 g.) in methanol (5 c.c.) was added and after 12 hr. at room temperature the reaction was completed by 3 hours' refluxing. The product, isolated with ether, was refluxed for 1 hour with N-aqueous potassium hydroxide (25 c.c.); 1-decalone (320 mg.) was recovered from the neutral fraction, and the alkaline liquors yielded 1-*oxo*-2-*decalylacetic acid* (320 mg.) which separated from ether–light petroleum as colourless plates, m. p. 153—154° (Found: C, 68·7; H, 8·7. $C_{12}H_{18}O_3$ requires C, 68·5; H, 8·6%).

cis-9-*Decalylacetic Acid*.—Methyl 1-oxo-*cis*-9-decalylacetate (500 mg.), prepared as a colourless oil, b. p. 120° (bath)/0·01 mm., from the acid (X; R = H) by the action of either methanolic sulphuric acid or diazomethane, was reduced during 12 hr. with amalgamated zinc (7 g.), concentrated hydrochloric acid (25 c.c.), and acetic acid (1·5 c.c.). The *product*, isolated with ether, crystallised from aqueous ethanol or light petroleum in colourless needles, m. p. 115° (Found: C, 73·4; H, 10·6. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·3%). The *anilide* crystallised from aqueous alcohol or light petroleum in slender needles, m. p. 155—156° (Found: C, 79·7; H, 9·3; N, 5·4. $C_{18}H_{25}ON$ requires C, 79·7; H, 9·3; N, 5·2%). *cis*-9-Decalylacetic acid (150 mg.) was dehydrogenated in an apparatus similar to that described by Linstead and Thomas,[15] with 30% palladium–charcoal on glass wool as catalyst at 325°; naphthalene (25 mg.) was isolated and identified by m. p. and mixed m. p.

XUM

cis-*Decalin*-9-*carboxylic Acid*.—(a) *From* cis-9-*decalylacetic acid*. Methyl *cis*-9-decalylacetate (415 mg.), prepared by action of diazomethane on the acid, was added in dry ether (25 c.c.) to a solution of phenylmagnesium bromide, prepared from bromobenzene (4·77 g.), magnesium (0·72 g.), and ether (20 c.c.). After 2½ hours' refluxing, the mixture was evaporated, benzene (30 c.c.) was added and the refluxing continued for a further 2½ hr. The mixture was acidified and the neutral product adsorbed on a column of alumina (30 g.) prepared in light petroleum. Elution with the same solvent gave diphenyl (480 mg.) and then an oil (360 mg.) which was heated with acetic anhydride (10 c.c.) for 20 min. The solvent was removed under reduced pressure, and the residue dissolved in acetic acid (15 c.c.) and oxidised during 24 hr. by chromic anhydride (253 mg.) in water (3 c.c.). Excess of oxidising agent was destroyed with ethanol and the solution evaporated under reduced pressure. The residual gum was shaken with ether and water, and the *acid* (75 mg.) removed from the ether layer by sodium hydrogen carbonate was recovered; it crystallised from aqueous ethanol in needles (33 mg.), m. p. 121—122° (Found: C, 72·7; H, 10·1. $C_{11}H_{18}O_2$ requires C, 72·5; H, 10·0%).

(b) *From* cis-10-*hydroxymethyl*-2-*decalone* (XII). The ketone [18] (XII) (1·60 g.) was reduced with amalgamated zinc (10 g.) and concentrated hydrochloric acid (25 c.c.). Extraction with ether gave crude 9-(hydroxymethyl)-*cis*-decalin (1·11 g.), b. p. (bath), 150—170°/10 mm., which crystallised on storage but was not purified further. Oxidation of the oil (350 mg.) in acetic acid (15 c.c.) with chromic anhydride (314 mg.) in water (1 c.c.) gave *cis*-decalin-9-carboxylic acid (30 mg.), m. p. 121—122°, alone or mixed with a specimen prepared by method (a).

*Perhydro*-2-*oxobenz*[d]*indole* (XV).—Methyl 1-oxo-9-decalylacetate (700 mg.), formamide (25 c.c.), and 98% formic acid (5 c.c.) were boiled under conditions which permitted excape of water. When the temperature of the fluid reached 190° the mixture was refluxed for 12 hr., then poured into water. The *product* (XV) (590 mg.) had m. p. 183—185° and separated from *cyclo*hexane in small needles, m. p. 189° (Found: C, 74·6; H, 9·9; N, 7·2. $C_{12}H_{19}ON$ requires C, 74·5; H, 9·9; N, 7·2%).

*Perhydrobenz*[d]*indole* (III; R = H).—A solution of lactam (XV) (460 mg.) in tetrahydrofuran (100 c.c.) was refluxed for 12 hr. with lithium aluminium hydride (410 mg.). After removal of the bulk of the solvent, water was added and the mixture extracted continuously with ether during 4 hr. Unchanged lactam (XV) (123 mg.) was recovered from the ether, and the base (III; R = H) removed in dilute hydrochloric acid and recovered as a brown oil (347 mg.). The *hydrobromide*, prepared with hydrogen bromide in ether, separated from acetone–ether in small colourless needles, m. p. 215° (Found: C, 55·0; H, 8·3; N, 5·7; Br, 30·8. $C_{12}H_{21}N,HBr$ requires C, 55·4; H, 8·5; N, 5·4; Br, 30·7%). The base (III; R = H), recovered from the hydrobromide as an oil, gave a positive Liebermann test.

*Perhydro*-3-*methylbenz*[d]*indole* (III; R = Me).—A mixture of the secondary base (III; R = H) (154 mg.), 98% formic acid (2 c.c.), and 40% formaldehyde (2 c.c.) was heated on a steam-bath for 12 hr. Concentrated hydrochloric acid (0·4 c.c.) was added, the solution was evaporated to dryness under reduced pressure, and the residue taken up in water and filtered, and the base recovered and isolated with ether. The crude brown oil (147 mg.), warmed with methyl iodide in hot acetone, gave a *methiodide* which separated from acetone–ether in small needles, m. p. 244° (Found: C, 50·2; H, 7·8; N, 4·2; I, 37·5. $C_{14}H_{26}NI$ requires C, 50·1; H, 7·8; N, 4·1; I, 37·8%).

1 : 2 : 3 : 5 : 6 : 6a : 7 : 8 : 9 : 10-*Decahydro*-2-*oxobenz*[d]*indole* (XVI).—Methyl 1-oxo-9-decalylacetate (from 700 mg. of acid) and ethanolic ammonia (40 c.c.; saturated at 0°) were heated in a sealed tube at 120° for 12 hr. Evaporation gave a brown gum which was adsorbed on a column of alumina (18 g.) prepared in benzene. On elution the column gave, to ether, crystals " a " (145 mg.); to chloroform, crystals " b " (120 mg.) followed by an oil (20 mg.); to methanol–chloroform (5% v/v), crystals " c " (292 mg.); and to methanol, an oil (48 mg.). Crystals " c " separated from *cyclo*hexane in slender rods, m. p. 184°, of the *lactam* (XVI) (Found: C, 74·8; H, 9·0; N, 7·2. $C_{12}H_{17}ON$ requires C, 75·3; H, 9·0; N, 7·3%), which were reduced by hydrogen in presence of 10% palladium–charcoal to perhydro-2-oxobenz[*d*]indole (XV), m. p. 188°. Crystals " a " and " b " were combined; recrystallisation from ligroin gave needles, m. p. 136—138°, which on further recrystallisation from ligroin separated into slender rods, m. p. 184°, of the unsaturated lactam (XVI) mentioned above, and long thin needles, m. p. 138—139°, which could not be purified. These needles were probably the amide of acid (X; R = H) and on attempted purification were converted into the lactam (XVI).

2 : 3 : 4 : 6 : 7 : 7a : 8 : 9 : 10 : 11-*Decahydro*-2-*oxo*-1H-*benzo*[e]*cinnoline* (XVII).—Methyl

1-oxo-9-decalylacetate (120 mg.) and 100% hydrazine hydrate (0·5 c.c.) in sufficient methanol to produce homogeneity were refluxed for 1½ hr., then cooled and the *product* (XVII) (80 mg.) was collected and crystallised first from benzene and then from *cyclo*hexane; it formed small needles, m. p. 204—205° (Found: C, 69·4; H, 8·9; N, 13·7. $C_{12}H_{18}ON_2$ requires C, 69·8; H, 8·8; N, 13·6%). This cyclic hydrazide reacted with nitrous acid in acetic acid solution at 0°, yielding a yellow crystalline *N*-nitroso-compound which gave a positive Liebermann reaction.

*Reduction of* 1-*Oxo*-cis-9-*decalylacetic Acid*.—(a) *With aluminium* iso*propoxide*. A mixture of methyl 1-oxo-*cis*-9-decalylacetate (200 mg.) and a molar solution of aluminium *iso*propoxide in propan-2-ol (15 c.c.) was slowly distilled during 4 hr., then concentrated under reduced pressure and boiled with excess of dilute hydrochloric acid. The product, isolated with ether, was a yellow oil (210 mg.) which yielded to sodium hydrogen carbonate solution unchanged 1-oxo-9-decalylacetic acid (69 mg.) and a neutral oil (91 mg.) which was hydrolysed by 1 hour's boiling with N-aqueous-methanolic potassium hydroxide (20 c.c.) to trans-1-*hydroxy*-cis-9-*decalylacetic acid* (XIX). This hydroxy-acid crystallised from light petroleum containing a little ether in slender needles (88 mg.), m. p. 118° (Found: C, 67·7; H, 9·1. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%), which gave an oily lactone from which the hydroxy-acid was recovered.

(b) *With hydrogen in presence of platinic oxide*. Reduction in acetic acid gave similar results to those outlined in (a).

(c) *With sodium borohydride*. To a solution of 1-oxo-*cis*-9-decalylacetic acid (1 g.) in 0·1N-sodium hydroxide (15 c.c.) was added a solution of sodium borohydride (400 mg.) in water (10 c.c.). The solution was boiled for 1 hr., cooled to 0°, covered with ether, and acidified with dilute hydrochloric acid. The ether extract yielded to sodium hydrogen carbonate solution *trans*-1-hydroxy-*cis*-9-decalylacetic acid (XIX) (540 mg.), m. p. 118°, and retained cis-1-*hydroxy*-cis-9-*decalylacetic lactone* (cf. XVIII) (403 mg.) which separated from light petroleum as prisms, m. p. 66° (Found: C, 74·1; H, 9·4. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%), $\nu_{max.}$ (KBr disc) 1780 cm.$^{-1}$. The lactone dissolved in warm dilute sodium hydroxide solution, but the corresponding hydroxy-acid could not be isolated, and attempts to oxidise the lactone with permanganate, hypobromite, and chromic acid in acetic acid or pyridine were unsuccessful. The lactone was recovered after 5 days at 85° in a sealed tube with methanolic ammonia (saturated at room temperature).

*Perhydro-3-oxobenz*[e]1 : 3-*benzoxazine* (XXI).—Methyl *trans*-1-hydroxy-*cis*-9-decalylacetate, prepared from the acid (XIX) (150 mg.) and ethereal diazomethane, was refluxed by 1½ hr. with 100% hydrazine hydrate (7 drops) and a little methanol. After dilution with water and acidification with dilute hydrochloric acid, neutral matter was removed in ether, and the base liberated with aqueous ammonia was taken up in ether and recovered as an oil (145 mg.) which partly crystallised but was not purified. The basic oil (145 mg.) was dissolved in excess of dilute hydrochloric acid, sodium nitrite (58 mg.) was added, the product taken up in ether and washed with sodium hydrogen carbonate solution, and benzene (10 c.c.) added. Evaporation to dryness gave the cyclic urethane (XXI) as crystals (75 mg.), which recrystallised from benzene–ligroin in small needles, m. p. 183° (Found: C, 68·5; H, 9·0; N, 6·8. $C_{13}H_{19}O_2N$ requires C, 68·9; H, 9·1; N, 6·7%).

trans-1-*Hydroxy*-cis-9-*decalylacetamide*.—Methyl *trans*-1-hydroxy-*cis*-9-decalylacetate, prepared from the acid (XIX) (403 mg.), was heated with methanolic ammonia (40 c.c., saturated at room temperature) for 11 hr. at 90° in a sealed tube. The solvent was removed under reduced pressure and the crystalline *amide* recrystallised from acetone in needles (330 mg.), m. p. 223° (Found: C, 68·5; H, 9·7; N, 7·0. $C_{12}H_{21}O_2N$ requires C, 68·2; H, 10·0; N, 6·6%). The amide was also obtained by allowing the ester and methanolic ammonia to react for 10 days at room temperature.

9-*Aminomethyl*-trans-1-*hydroxy*-cis-*decalin* (XX).—A solution of sodium methoxide, from sodium (39 mg.) and methanol (3 c.c.), was added to a suspension of *trans*-1-hydroxy-*cis*-9-decalylacetamide (153 mg.) in methanol (10 c.c.), and a solution of bromine (116 mg.) in methanol (3 c.c.) was introduced. The amide rapidly dissolved and reaction was completed by 15 minutes' boiling, after which 40% aqueous potassium hydroxide (1·5 c.c.) was added, the mixture was refluxed for 12 hr., diluted, and acidified, and neutral matter removed in ether. Basification and continuous ether-extraction of the aqueous layer yielded the *base* (XX) which separated from ligroin in slender needles (90 mg.), m. p. 106—107° (Found, in sample dried over KOH at 56°/0·1 mm.: C, 71·6; H, 11·2; N, 7·8. $C_{11}H_{21}ON$ requires C, 72·0; H, 11·5; N, 7·6%).

XUM

The *hydrochloride*, prepared in benzene, separated from ligroin containing a little chloroform in small needles, m. p. 213—214° (Found: C, 59·7; H, 10·1; N, 6·8; Cl, 15·7. $C_{11}H_{21}ON,HCl$ requires C, 60·0; H, 10·1; N, 6·4; Cl, 16·1%). The N-*acetyl derivative* separated from ligroin containing a little benzene in needles, m. p. 128° (Found: C, 69·3; H, 9·7; N, 6·4. $C_{13}H_{23}O_2N$ requires C, 69·3; H, 10·3; N, 6·2%).

9-(N-*Cyanomethylaminomethyl*)-trans-1-*hydroxy*-cis-*decalin* (XXII; R = H).—Aqueous formaldehyde (0·04 c.c. of 40%) was added to a concentrated aqueous solution of the hydrochloride (110 mg.) of base (XX). The solution was covered with ether and cooled to 0°, and concentrated aqueous potassium cyanide (33 mg.) added. After 12 hours' shaking a little saturated sodium chloride solution was added. The product (XXII; R = H), isolated with ether, was an oil (95 mg.). The *hydrochloride*, prepared in ether, separated from methanol–benzene in needles, m. p. 193—194° (decomp.) (Found: C, 59·6; H, 8·8; N, 10·9; Cl, 14·2. $C_{13}H_{23}ON_2,HCl$ requires C, 60·3; H, 9·0; N, 10·8; Cl, 13·7%).

9-(N-*Cyanomethyl*-N-*methylaminomethyl*)-trans-1-*hydroxy*-cis-*decalin* (XXII; R = Me).—The secondary base (XXII; R = H) (164 mg.) was refluxed for 12 hr. with 90% formic acid (1 c.c.) and 40% aqueous formaldehyde (1 c.c.). After addition of concentrated hydrochloric acid (0·1 c.c.) and evaporation to dryness, the residue was taken up in dilute hydrochloric acid, and neutral impurities were removed by filtration and continuous extraction with ether for 2 hr. The base (XXII; R = Me), isolated from the acid layer by basification with ammonia and extraction with ether, was an oil (115 mg.), which with an excess of methyl iodide in boiling acetone gave a methiodide as needles (from acetone), m. p. 242° (Found: C, 47·8; H, 7·3; N, 7·3; I, 33·9. $C_{15}H_{27}ON_2I$ requires C, 47·6; H, 7·2; N, 7·4; I, 33·6%).

We thank the Department of Scientific and Industrial Research for a Maintenance Grant, and Imperial Chemical Industries Limited for a grant towards the expenses of the research.

DEPARTMENT OF CHEMISTRY,
THE UNIVERSITY, SHEFFIELD, 10. [*Received, November 12th*, 1957.]

---

## 245. *The Synthesis of Some Substituted Hexahydro-12-methyl-2-oxophenanthrenes.*

By F. H. HOWELL and D. A. H. TAYLOR.

3 : 4-Dihydro-1-methylnaphthalene with perbenzoic acid (cf. ref. 1) gives 1-methyl-2-tetralone, which has been converted into 2 : 3 : 4 : 9 : 10 : 12-hexahydro-12-methyl-2-oxophenanthrene.[2] The method has been shown to be applicable to several derivatives.

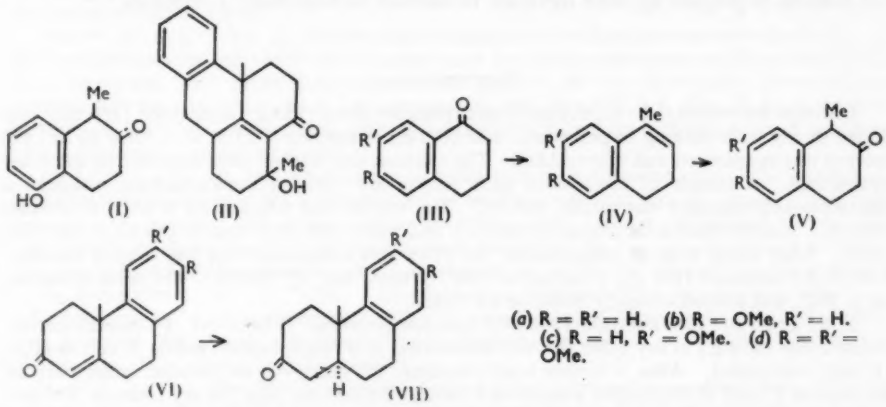
THE Robinson ring-extension gives a good yield when applied to 1-methyl-2-tetralones, and is a satisfactory way of making intermediate substances for the synthesis of several natural products.[3-6] However, although 2-tetralones are easily made, monomethylation is difficult by ordinary methods.[3,4,6,7] Cornforth and Robinson have avoided this difficulty in the case of 5-hydroxy-1-methyl-2-tetralone (I) which has been made directly by the reduction of 6-methoxy-5-methyl-1-naphthol,[7] but the starting material is not easy to obtain, and some of the stages are limited in scale.

An interesting approach is the oxidation of 4-alkyl-1 : 2-dihydronaphthalenes, first explored by Ghosh and Robinson [8] and lately described by Newhall *et al.*[5] in the specific case of 5-hydroxy-8-methoxy-1-methyl-2-tetralone. Both groups found perbenzoic acid

[1] English and Cavaglieri, *J. Amer. Chem. Soc.*, 1943, **65**, 1085.
[2] Zwahlen, Horton, and Fujimoto, *J. Amer. Chem. Soc.*, 1957, **79**, 3131.
[3] Cornforth and Robinson, *J.*, 1946, 676.
[4] Grob and Jundt, *Helv. Chim. Acta*, 1952, **35**, 2111.
[5] Newhall, Harris, Holly, Johnston, Richter, Walton, Wilson, and Folkers, *J. Amer. Chem. Soc.*, 1955, **77**, 5646.
[6] Stork and Schulenberg, *ibid.*, 1956, **78**, 250.
[7] Cornforth, Kauder, Pike, and Robinson, *J.*, 1955, 3348.
[8] Ghosh and Robinson, *J.*, 1944, 506.

XUM

unsatisfactory; Ghosh and Robinson got a low yield with hydrogen peroxide in acetic acid, while the Merck group found red lead in acetic acid very satisfactory. English and Cavaglieri [1] described the oxidation of 1 : 2-dihydro-4-methylnaphthalene to 1-methyl-2-tetralone with perbenzoic acid, and we found this a very good preparative method. It is stated that the oxidation yields the ketone directly without accompanying epoxide, but we find the product often gives only a little semicarbazone, although a dinitrophenylhydrazone is formed in good yield. As our crude product has a roughly constant boiling point (the




same as that of the ketone), we suppose the non-ketonic material is the epoxide and not the glycol monobenzoate. It is easily converted into the ketone by dilute acid. Performic acid, perphthalic acid, and red lead in acetic acid gave unsatisfactory results.

For the ring extension of 1-methyl-2-tetralone, we found alkylation with 4-chlorobutan-2-one in the presence of sodium hydride in light petroleum gave the best yield, a method which seems not to have been used before. Ring extension, using the Mannich base, gave also a by-product, $C_{19}H_{22}O_2$, m. p. 166°. The spectrum of this shows that it is an αβ-unsaturated ketone. It may have the structure (II) and arise from dialkylation of 1-methyl-2-tetralone.

We have reduced 2 : 3 : 4 : 9 : 10 : 12-hexahydro-12-methyl-2-oxophenanthrene (VI*a*) in several ways. Lithium in liquid ammonia gave a 60% yield of a crystalline ketone (VII*a*) which we suppose is the more stable *trans*-isomer. With lithium aluminium hydride this gave an oily alcohol, having a crystalline benzoate in which the hydroxyl group should have the more stable equatorial 2β-conformation. Catalytic reduction of the ketone (VI*a*) gave oils containing more or less of the *cis*-isomer; on further reduction with lithium aluminium hydride a crystalline alcohol was obtained to which we assign the 2α-*cis*-structure. Re-oxidation of this gave the oily *cis*-ketone, isolated as its semicarbazone. The nuclear structure of this alcohol was confirmed by dehydrogenation to phenanthrene over a palladium catalyst.

6-Methoxy-1-tetralone, 7-methoxy-1-tetralone, and 6 : 7-dimethoxy-1-tetralone are readily obtained. We have converted them into the corresponding 1-methyl-2-tetralones without difficulty. The structure of the crystalline 1 : 2-dihydro-6 : 7-dimethoxy-4-methylnaphthalene (IV*d*) was proved by acetylation to the known 3-acetyl derivative. 6 : 7-Dimethoxy-1-methyl-2-tetralone (V*d*) was also obtained crystalline, and an attempt was made to prove the structure by reaction with ethylmagnesium bromide and dehydrogenation to 2-ethyl-6 : 7-dimethoxy-1-methylnaphthalene. Only 6 : 7-dimethoxy-1-methyl-2-naphthol was obtained, so it seems that the ketone reacted with the Grignard reagent completely in the enolic form.

Ring extension of these three 2-tetralones then gave respectively the oxophenanthrenes

(VI*b*, *c*, and *d*), the best yield in each case being obtained by the Mannich base method. Reduction with lithium in liquid ammonia gave the *trans*-ketones (VII*b*, *c*, and *d*), of which only the 6-methoxy-compound (VII*c*) crystallised. All the alcohols have remained amorphous. The use of these compounds in the preparation of substances related to natural products will be described shortly.

This method also affords 5-methoxy-1-methyl-2-tetralone, which has interest as the intermediate in the Robinson–Cornforth steroid synthesis. This substance is, however, not difficult to prepare by other methods, in contrast to 5-methoxy-1-tetralone.[9,10]

## Experimental

1-*Methyl*-2-*tetralone*.—1 : 2-Dihydro-4-methylnaphthalene (130 g.) in acetone (400 ml.) was added slowly with shaking to perbenzoic acid (130 g.) in acetone (1 l.) at 0°. After 2½ hr., the solvent was evaporated and ether added. The solution was washed until neutral and the ether evaporated. A sample of the residue gave only a low yield of semicarbazone, although a dinitrophenylhydrazone was readily formed. The residue was refluxed for 4 hr. with ethanol (800 ml.), concentrated sulphuric acid (100 ml.), and water (600 ml.), cooled, and extracted with ether. After being washed until neutral, the ether was evaporated and the residue distilled. 1-Methyl-2-tetralone (107 g.), collected at 128°/14 mm., had $n_D^{20}$ 1·5568. The semicarbazone, m. p. 202°, was formed in nearly quantitative yield.

2 : 3 : 4 : 9 : 10 : 12-*Hexahydro*-12-*methyl*-2-*oxophenanthrene* (VI*a*).—(*a*) 4-Dimethylaminobutan-2-one (20·5 g.) in dry ether (25 ml.) was stirred at 0° while methyl iodide (9 ml.) in ether (10 ml.) was added. After a further hour's stirring, the ether was evaporated under reduced pressure at 0°, and to the residue was added 1-methyl-2-tetralone (22 g.) in dry benzene (100 ml.) and then potassium (7 g.) in ethanol (100 ml.), then the whole was stirred for 2 hr. at 0° and 10 min. on the steam-bath. Dilute sulphuric acid and ether were added, and the organic layer was washed until neutral. Evaporation of the solvent and distillation of the residue gave 2 : 3 : 4 : 9 : 10 : 12-hexahydro-12-methyl-2-oxophenanthrene, b. p. 144—146°/0·05 mm., which crystallised from light petroleum (b. p. 60—80°) as prisms, m. p. 90° (3·5 g.) (Zwahlen *et al.*[2] give m. p. 90—91°) (Found: C, 84·5; H, 7·4. Calc. for $C_{15}H_{16}O$: C, 84·8; H, 7·6%), $\nu$ 1669 cm.$^{-1}$ (in Nujol). The *semicarbazone* formed prisms, m. p. 220—224°, from ethanol (Found: C, 72·0, 71·3; H, 7·3, 6·9; N, 15·6. $C_{16}H_{19}ON_3$ requires C, 71·3; H, 7·1; N, 15·6%). A fraction, collected at 150—200°/0·05 mm., crystallised from acetone–light petroleum (b. p. 60—80°), giving a *substance* as prisms (1·2 g.), m. p. 166° (Found: C, 80·3; H, 7·9. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·8%), $\lambda_{max.}$ 247 m$\mu$ (log $\varepsilon$ 4·15 in EtOH), $\nu$ 1669 cm.$^{-1}$ (in Nujol). The *semicarbazone* formed very insoluble crystals, m. p. 268—270°, from ethanol (Found: C, 71·2; H, 7·7. $C_{20}H_{25}O_2N_3$ requires C, 70·8; H, 7·4%). A third *substance* (200 mg.), obtained by storing the residues in light petroleum (b. p. 60—80°), had m. p. 198° (from benzene) (Found: C, 77·1; H, 6·9. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·8%), $\nu$ 1720 cm.$^{-1}$.

(*b*) 1-Methyl-2-tetralone (16 g.) was added to sodium hydride (2·5 g.) in light petroleum (b. p. 60—80°; 100 ml.). The suspension was stirred while 4-chlorobutan-2-one (11 g.) was added rapidly. After the initial reaction was over, refluxing was continued for 15 min., the whole was cooled, and sodium hydride (2·5 g.) added. After ½ hour's refluxing, dilute hydrochloric acid was added, the organic layer separated and evaporated, and the residue distilled. The tricyclic ketone was collected at 160°/0·1 mm. and formed colourless prisms (11·0 g.), m. p. and mixed m. p. 90°, from light petroleum (b. p. 60—80°). Chromatography of the mother-liquors gave a further amount (total 70%).

*Reduction of the Tricyclic Ketone* (VI*a*).—(a) *Over palladised calcium carbonate.* The ketone (300 mg.) in ethanol (10 ml.) was shaken with hydrogen over palladised calcium carbonate for 2 hr. Filtration, evaporation, and recrystallisation from light petroleum (b. p. 60—80°) gave trans-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydro*-12-*methyl*-2-*oxophenanthrene* (VII*a*) (15 mg.) as plates, m. p. 106—107° (Found: C, 83·9; H, 8·3. $C_{15}H_{18}O$ requires C, 84·1; H, 8·5%). The *semicarbazone* formed needles, m. p. 229—231° (decomp.), from ethanol (Found: C, 71·4, 70·8; H, 7·4, 7·2; N, 15·6. $C_{16}H_{21}ON_3$ requires C, 70·8; H, 7·8; N, 15·5%).

[9] Lockett and Short, *J.*, 1939, 787.
[10] Papa, Schwenk, and Breiger, *J. Org. Chem.*, 1949, **14**, 366.

(b) *Over palladised alumina.* The tricyclic ketone (600 mg.), reduced in ethanol (25 ml.) and concentrated hydrochloric acid (3 drops) over palladised alumina, gave the *trans*-ketone (110 mg.), m. p. 106—107°, undepressed on admixture with the previous sample.

(c) *With lithium in liquid ammonia.* Lithium (300 mg.) was dissolved in liquid ammonia (100 ml.), and the tricyclic ketone (1·5 g.) in dry ether (50 ml.) added. After 15 min. ammonium chloride was added, and then, after evaporation of most of the ammonia, also ether and water. Evaporation of the ether layer left crystals which gave the *trans*-ketone (900 mg. 60%), m. p. and mixed m. p. 106°, from light petroleum (b. p. 60—80°). The use of calcium in place of lithium gave similar results.

trans-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro*-2β-*hydroxy*-12-*methylphenanthrene*.—Reduction of the *trans*-ketone (500 mg.) with lithium aluminium hydride in ether gave an oily alcohol which on benzoylation gave trans-2β-*benzoyloxy*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydro*-12-*methylphenanthrene* (500 mg.) as prisms, m. p. 160° (Found: C, 81·9, 82·4; H, 7·4, 7·3. $C_{22}H_{24}O_2$ requires C, 82·5; H, 7·5%). This benzoate (195 mg.) was also obtained on hydrogenation of the *trans*-ketone (200 mg.) over Adams catalyst.

cis-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro*-2α-*hydroxy*-12-*methylphenanthrene*.—The amorphous saturated ketone obtained by hydrogenation at neutral palladium [see (*a*) above] (7·0 g.) was reduced with lithium aluminium hydride in ether. The product crystallised slowly from light petroleum (b. p. 60—80°); recrystallisation gave cis-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydro*-2α-*hydroxy*-12-*methylphenanthrene* (1·9 g.) as needles, m. p. 75—77° (Found: C, 83·5; H, 9·4. $C_{15}H_{20}O$ requires C, 83·3; H, 9·3%). The *benzoate* crystallised from ethanol in prisms, m. p. 155—156°, giving a large depression with the *trans*-benzoate (Found: C, 82·4; H, 7·6%). This benzoate (50%) was also obtained on hydrogenation of the unsaturated ketone over Adams catalyst or Raney nickel in ethanol.

cis-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro*-12-*methyl*-2-*oxophenanthrene*.—Oxidation of the *cis*-alcohol with chromic acid in acetone by the procedure of Bowers *et al.*[11] gave the oily *cis*-ketone which gave a *semicarbazone* as prisms, m. p. 196—198° (decomp.), from ethanol (Found: C, 71·0; H, 7·7; N, 15·7. $C_{16}H_{21}ON_3$ requires C, 70·8; H, 7·8; N, 15·5%).

*Dehydrogenation of the Crude* cis-*Alcohol*.—This alcohol (500 mg.) was heated for 4 hr. with 30% palladised charcoal (100 mg.) at 400°. Chromatography and sublimation, followed by two crystallisations from ethanol, gave phenanthrene (12 mg.), m. p. and mixed m. p. 98—100°.

6 : 7-*Dimethoxy*-1-*tetralone* (III*d*).—γ-(3 : 4-Dimethoxyphenyl)butyric acid (96 g.), benzene (500 ml.), and phosphorus pentachloride (100 g.) were refluxed for 1 hr., and the solution was washed until neutral and evaporated. Crystallisation of the residue from light petroleum (b. p. 60—80°) gave 6 : 7-dimethoxy-1-tetralone as prisms, m. p. 96°. The method of Haworth and Mavin [12] gave, in our hands, a product difficult to purify.

1 : 2-*Dihydro*-6 : 7-*dimethoxy*-4-*methylnaphthalene* (IV*d*) (cf. ref. 12).—6 : 7-Dimethoxy-1-tetralone (70 g.) in benzene (250 ml.) was added to a solution prepared from magnesium (12 g.) and excess of methyl bromide in ether (700 ml.). After ½ hour's refluxing, saturated ammonium chloride solution was added, and the ether layer separated and evaporated. Heating the residual alcohol dehydrated it and then crystallisation from light petroleum (b. p. 60—80°) gave 1 : 2-*dihydro*-6 : 7-*dimethoxy*-4-*methylnaphthalene* (60 g.), prisms, m. p. 70—72° (Found: C, 76·6; H, 7·9. $C_{13}H_{16}O_2$ requires C, 76·4; H, 7·9%). Heating the alcohol with formic acid gave 6 : 7-dimethoxy-1-methylnaphthalene, needles (from methanol), m. p. 114°. A sample made by decarboxylation of 6 : 7-dimethoxy-1-methylnaphthalene-2-carboxylic acid [13] with copper bronze in quinoline had m. p. and mixed m. p. 114° (Found: C, 77·2; H, 7·0. Calc. for $C_{13}H_{16}O_2$: C, 77·2; H, 7·0%). Haworth and Mavin give m. p. 110—111°.

2-*Acetyl*-3 : 4-*dihydro*-6 : 7-*dimethoxy*-1-*methylnaphthalene*.—1 : 2-Dihydro-6 : 7-dimethoxy-4-methylnaphthalene (4·0 g.) was treated in nitrobenzene (10 ml.) with acetyl chloride (1·5 ml.) and aluminium chloride (2·7 g.) in nitrobenzene (10 ml.). After being kept overnight the solution was poured into ice and hydrochloric acid, ether added, and the organic layer washed to neutrality and distilled. The fraction collected at 160—170°/0·5 mm. was taken up in ethanol, whereupon it crystallised. Recrystallisation gave 2-acetyl-3 : 4-dihydro-6 : 7-dimethoxy-1-methylnaphthalene (300 mg.) as pale yellow plates, m. p. 109°, alone or mixed with an authentic specimen [13] (Found: C 73·4; H, 7·3. Calc. for $C_{15}H_{18}O_3$: C, 73·1; H, 7·4%).

[11] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548.
[12] Haworth and Mavin, *J.*, 1932, 1485.
[13] Howell and Taylor, *J.*, 1956, 4252.

XUM

**6 : 7-*Dimethoxy*-1-*methyl*-2-*tetralone*** (V*d*).—1 : 2-Dihydro-6 : 7-dimethoxy-4-methylnaphthalene (35 g.) in chloroform (100 ml.) was treated with perbenzoic acid (36 g.) in chloroform (360 ml.). After storage overnight the solution was washed neutral and the residue distilled. The fraction collected at 160—175°/0·1 mm. crystallised from methanol, to give **6 : 7-*dimethoxy*-1-*methyl*-2-*tetralone*** (26 g.) as prisms, m. p. 87° (Found: C, 71·2; H, 6·95. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). The ***semicarbazone*** formed needles, m. p. 200° (decomp.), from ethanol (Found: C, 60·6; H, 7·1; N, 15·1. $C_{14}H_{19}O_3N_3$ requires C, 60·6; H, 6·9; N, 15·15%). A fraction collected at 180—200°/0·1 mm. crystallised from methanol, giving **6 : 7-*dimethoxy*-1-*methyl*-2-*naphthol*** (500 mg.), needles, m. p. 223° (Found: C, 71·6; H, 6·6. $C_{13}H_{14}O_3$ requires C, 71·5; H, 6·5%).

**6 : 7-*Dimethoxy*-1-*methyl*-2-*naphthol*.**—6 : 7-Dimethoxy-1-methyl-2-tetralone (900 mg.) in ether (50 ml.) was added to a Grignard solution prepared from magnesium (0·5 g.) and ethyl bromide (2 ml.) in ether (30 ml.). After 15 minutes' refluxing, the product was isolated and heated at 300° for ½ hr. with 30% palladised charcoa l(100 mg.). The solid product recrystallised from methanol, yielding 6:7-dimethoxy-1-methyl-2-naphthol (600 mg.), m. p. and mixed m. p. 223°.

**2-*Ethyl*-6 : 7-*dimethoxy*-1-*methylnaphthalene***.—2-Acetyl-6 : 7-dimethoxy-1-methylnaphthalene [13] (400 mg.) in toluene (10 ml.) was refluxed with amalgamated zinc (6 g.) in hydrochloric acid (9·0 ml.) and water (11 ml.) for 6 hr. Ether-extraction and evaporation gave a solid which was sublimed and then recrystallised from light petroleum (b. p. 60—80°). **2-*Ethyl*-6 : 7-*dimethoxy*-1-*methylnaphthalene*** (300 mg.) formed plates, m. p. 92—93° (Found: C, 78·2; H, 8·1. $C_{15}H_{18}O_2$ requires C, 78·2; H, 7·9%).

**2 : 3 : 4 : 9 : 10 : 12-*Hexahydro*-6 : 7-*dimethoxy*-12-*methyl*-2-*oxophenanthrene*** (VI*d*).—4-Dimethylaminobutan-2-one (14 g.) was dissolved in dry ether (50 ml.) and methyl iodide (8 ml.) added with stirring at 0°. After 1 hr. the ether was removed under reduced pressure at 0°, and 6 : 7-dimethoxy-1-methyl-2-tetralone (26 g.) in benzene (130 ml.) added. A solution of sodium (5·5 g.) in methanol (130 ml.) was added at 0° with stirring in a nitrogen atmosphere, and the mixture stirred for 2 hr., then refluxed for 10 min. Ether and dilute sulphuric acid were added, the organic layer was washed until neutral, and distilled. An oil (23 g.) was collected at 184—186°/0·01 mm. Crystallisation from ether gave **2 : 3 : 4 : 9 : 10 : 12-*hexahydro*-6 : 7-*dimethoxy*-12-*methyl*-2-*oxophenanthrene*** (19·2 g., 60%) as yellow prisms, m. p. 105—106° (Found: C, 74·5; H, 7·85. $C_{17}H_{20}O_3$ requires C, 75·0; H, 7·4%). The semicarbazone formed orange prisms, m. p. 232° (decomp.), from ethanol (Found: C, 65·5; H, 7·3; N, 12·85. $C_{18}H_{23}O_3N_3$ requires C, 65·6; H, 7·0; N, 12·8%).

**2 : 3 : 4 : 6 : 10 : 12-*Hexahydro*-6 : 7-*dihydroxy*-12-*methyl*-2-*oxophenanthrene***.—The dimethoxy-compound (1·0 g.) was refluxed for ½ hr. with acetic acid (20 ml.) and 55% hydriodic acid (4·0 ml.; prepared by refluxing over red phosphorus and filtering). Ether and water were added, and the ether layer was washed with aqueous sodium hydrogen sulphite solution and with water, and evaporated. The residue crystallised from a little ether, and recrystallisation from methanol–ether gave **2 : 3 : 4 : 9 : 10 : 12-*hexahydro*-6 : 7-*dihydroxy*-12-*methyl*-2-*oxophenanthrene*** (300 mg.) as unstable yellow prisms, m. p. 200° (decomp.), giving an intense green colour with ferric chloride (Found: C, 72·7; H, 6·7. $C_{15}H_{16}O_3$ requires C, 73·75; H, 6·6%).

**1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro*-6 : 7-*dimethoxy*-12-*methyl*-2-*oxophenanthrene*** (VII*d*).—The dimethoxy-compound (500 mg.) in dioxan (20 ml.) and ether (20 ml.) was added slowly to a solution of lithium (100 mg.) in liquid ammonia (50 ml.). After 15 min. ammonium chloride was added, the ammonia was evaporated, and ether and water were added. The ether layer was washed until neutral and evaporated; the oily residue gave the *semicarbazone* of the octahydro-compound as plates, m. p. 213—215° (decomp.), from ethanol (Found: C, 65·5; H, 7·7; N, 13·05. $C_{18}H_{25}O_3N_3$ requires C, 65·2; H, 7·6; N, 12·7%).

***7-Methoxy*-1-*tetralone*** (III*c*).—Succinic anhydride (100 g.), suspended in nitrobenzene (200 ml.) and anisole (108 g.), was added with shaking to a solution of aluminium chloride (266 g.) in nitrobenzene (600 ml.) at 0°. After storage overnight at room temperature, the solution was heated at 45° for 1 hr., then poured into ice and hydrochloric acid. The solid which separated was filtered off and reprecipitated from sodium carbonate solution. The acid obtained was reduced in the usual way by the Clemmensen method using toluene; distillation then gave γ-*p*-methoxyphenylbutyric acid (149 g.), b. p. 153—154°/0·05 mm., which was cyclised as described by Haworth and Sheldrick.[14] 7-Methoxy-1-tetralone (105 g., 60% calc. on anisole) was obtained as prisms, m. p. 66°.

[14] Haworth and Sheldrick, *J.*, 1934, 1950.

**1 : 2-*Dihydro-6-methoxy-4-methylnaphthalene*** (IV*c*).—7-Methoxy-1-tetralone (50 g.) in ether (400 ml.) was added slowly with stirring to a Grignard solution from methyl iodide (30 ml.) and magnesium (11 g.) in ether (400 ml.). After addition of saturated ammonium chloride solution the ether layer was removed and evaporated. The residue was heated with potassium hydrogen sulphate (50 g.) at 120° for 2 hr. The product was isolated with ether and distilled, 1 : 2-dihydro-6-methoxy-4-methylnaphthalene (43 g.) being collected at 145—148°/14 mm.

***7-Methoxy-1-methyl-2-tetralone*** (V*c*).—1 : 2-Dihydro-6-methoxy-4-methylnaphthalene (43 g.) was dissolved in chloroform (100 ml.), and perbenzoic acid (43 g.) in chloroform (600 ml.) added slowly with stirring at 0°. After being kept overnight at 0°, the solution was washed with sodium hydroxide solution and water and evaporated. The residue was refluxed in ethanol (300 ml.), water (250 ml.), and sulphuric acid (50 ml.) for 3 hr., then concentrated under reduced pressure. Ether was added and the solution washed until neutral and distilled. 7-*Methoxy-1-methyl-2-tetralone* (34 g., 71%) was collected at 120—122°/0·1 mm. (Found: C, 75·5; H, 7·5. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%). The *semicarbazone* crystallised from ethanol in needles, m. p. 197° (decomp.) (Found: C, 63·4; H, 6·6; N, 16·9. $C_{13}H_{17}O_2N_3$ requires C, 63·1; H, 6·9; N, 17·0%).

**2 : 3 : 4 : 9 : 10 : 12-*Hexahydro-6-methoxy-12-methyl-2-oxophenanthrene*** (VI*c*).—4-Dimethylaminobutan-2-one (21 g.) in ether (75 ml.) was cooled to 0° and methyl iodide (11·5 ml.) in ether (15 ml.) added with stirring in 15 min. After 1 hour's stirring at 0°, the solution was evaporated under reduced pressure, and 7-methoxy-1-methyl-2-tetralone (34 g.) in benzene (200 ml.) was added under nitrogen. A solution from sodium (8·2 g.) and methanol (200 ml.) was added in 5 min. and the whole stirred for 2 hr. at 0°, then 10 min. at the b. p. Ether and dilute sulphuric acid were added, and the ether layer was washed until neutral and distilled. A pale yellow oil (31·4 g.) was collected at 186—187°/0·01 mm., which crystallised from ether–light petroleum (b. p. 60—80°) to give **2 : 3 : 4 : 9 : 10 : 12-*hexahydro-6-methoxy-12-methyl-2-oxophenanthrene*** (21·7 g., 50%) as prisms, m. p. 63° (Found: C, 79·8; H, 7·8. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·5%). The *semicarbazone* formed prisms, m. p. 218—220° (decomp.), from ethanol (Found: C, 68·2; H, 7·0; N, 14·5. $C_{17}H_{21}O_2N_3$ requires C, 68·2; H, 7·1; N, 14·0%).

**1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro-6-methoxy-12-methyl-2-oxophenanthrene*** (VII*c*).—The preceding ketone (10 g.) in ether (200 ml.) was added to liquid ammonia (400 ml.) containing lithium (1 g.). After 5 min. ammonium chloride was added, the ammonia evaporated, and the ether solution washed until neutral and evaporated. The residue, crystallised from ether, gave the *octahydro-ketone* (7·8 g.) as prisms, m. p. 130° (Found: C, 78·4; H, 8·3. $C_{16}H_{20}O_2$ requires C, 78·65; H, 8·25%). The *semicarbazone* formed plates, m. p. 208—210° (decomp.), from ethanol (Found: C, 67·3; H, 7·4; N, 14·1. $C_{17}H_{23}O_2N_3$ requires C, 67·75; H, 7·7; N, 13·9%).

**2 : 3 : 4 : 9 : 10 : 12-*Hexahydro-6-hydroxy-12-methyl-2-oxophenanthrene***.—The preceding hexahydro-methoxy-ketone (500 mg.) was heated in acetic acid (9 ml.) and 55% hydriodic acid (1 ml.; cf. above) for ½ hr. Treatment with ether, washing with sodium hydrogen sulphite solution, removal of the phenol with sodium hydroxide solution, and its sublimation at 160—170°/0·02 mm. and crystallisation from ether afforded **2 : 3 : 4 : 9 : 10 : 12-*hexahydro-6-hydroxy-12-methyl-2-oxophenanthrene*** (340 mg.) as bright yellow plates, m. p. 202° (Found: C, 78·7; H, 7·2. $C_{15}H_{16}O_2$ requires C, 78·9; H, 7·1%).

***6-Methoxy-1-methyl-2-tetralone*** (V*b*).—To a Grignard solution from magnesium (6 g.) and methyl iodide (15 ml.) in ether (500 ml.), 6-methoxy-1-tetralone (27 g.) in ether (400 ml.) was added slowly with stirring. The complex was decomposed with saturated ammonium chloride solution, and the ether layer washed with water and evaporated. The residue was heated with potassium hydrogen sulphate (30 g.) for 2 hr. at 120—130°, ether and water were added, the ether layer was washed and evaporated, and the residue distilled. 1 : 2-Dihydro-7-methoxy-4-methylnaphthalene (20·2 g.) was collected at 148—154°/14 mm. This was treated in chloroform (75 ml.) with perbenzoic acid (28 g.) in chloroform (280 ml.) at 0°. The solution was kept overnight at 0°, washed, and evaporated. The residue was refluxed for 3 hr. with water (125 ml.), ethanol (150 ml.), and concentrated sulphuric acid (25 ml.), and the product isolated with ether and distilled. 6-Methoxy-1-methyl-2-tetralone (10 g.) was collected at 120—128°/0·05 mm. The *semicarbazone* formed needles, m. p. 218—220° (decomp.), from ethanol (Found: C, 63·2; H, 6·7; N, 16·4. $C_{13}H_{17}O_2N_3$ requires C, 63·1; H, 6·9; N, 17·0%). A fraction, b. p. 130—170°/0·01 mm., crystallised from aqueous ethanol to give ***6-methoxy-1-methyl-2-naphthol*** (600 mg.), needles, m. p. 154° (Found: C, 76·5; H, 6·6. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%).

XUM

2 : 3 : 4 : 9 : 10 : 12-*Hexahydro*-7-*methoxy*-12-*methyl*-2-*oxophenanthrene* (VI*b*).—4-Dimethylaminobutan-2-one (6 g.) in ether (20 ml.) was cooled to 0° and methyl iodide (3·3 ml.) in ether (10 ml.) was added in 15 min. After 1 hour's stirring at 0°, the ether was removed under reduced pressure and 6-methoxy-1-methyl-2-tetralone (9·8 g.) was added in benzene (60 ml.) under nitrogen. A solution of sodium (2·4 g.) in methanol (60 ml.) was added in 5 min., and the whole stirred for 2 hr. at 0° and then for 10 min. at the b. p. The product (5·4 g.) had b. p. 180—188°/0·3 mm. and gave 2 : 3 : 4 : 9 : 10 : 12-*hexahydro*-7-*methoxy*-12-*methyl*-2-*oxophenanthrene* (2·9 g.) as pale yellow prisms, m. p. 106—108°, from ether (Found: C, 79·1; H, 7·7. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·5%). The *semicarbazone* formed plates, m. p. 233—236° (decomp.), from ethanol (Found: C, 68·0; H, 6·85; N, 14·2. $C_{17}H_{21}O_2N_3$ requires C, 68·2; H, 7·1; N, 14·0%). The *trans*-octahydro-derivative, prepared with lithium and liquid ammonia in the usual way, failed to crystallise, but its *semicarbazone* formed prisms, m. p. 232—233° (decomp.), from ethanol (Found: C, 67·85; H, 7·6; N, 14·2. $C_{17}H_{23}O_2N_3$ requires C, 67·75; H, 7·7; N, 13·9%).

2 : 3 : 4 : 9 : 10 : 12-*Hexahydro*-8-*methoxy*-12-*methyl*-2-*oxophenanthrene*.—5-Methoxy-1-tetralone (1 g.) was added to a Grignard solution prepared from magnesium (1 g.) and methyl iodide (1 ml.) in ether (20 ml.). The complex was decomposed with aqueous ammonium chloride, and the ether layer evaporated. The residue was heated for 2 hr. at 130° with potassium hydrogen sulphate (1 g.), and the product isolated with ether and distilled. 1 : 2-Dihydro-8-methoxy-4-methylnaphthalene (850 mg.) was collected at 180° (bath) /15 mm. This was added in chloroform (10 ml.) to perbenzoic acid (1 g.) in chloroform (20 ml.). After being kept overnight at 0° the solution was washed to neutrality and evaporated. The residue was refluxed for 3 hr. with ethanol (25 ml.), water (25 ml.), and sulphuric acid (2·5 ml.), and the product isolated with ether. Distillation gave 5-methoxy-1-methyl-2-tetralone, b. p. 220° (bath)/15 mm. Potassium (200 mg.) was dissolved in *tert.*-butyl alcohol (200 ml.), and the tetralone added, followed by 4-chlorobutan-2-one (316 mg.). After ½ hour's refluxing, dilute hydrochloric acid was added and the product isolated with ether and chromatographed on alumina (12 g.; Spence type " H "). *cyclo*Hexane containing 10% of benzene eluted an oil which, crystallised from *cyclo*hexane, gave 2 : 3 : 4 : 9 : 10 : 12-hexahydro-8-methoxy-12-methyl-2-oxophenanthrene (80 mg.) as pale yellow prisms, m. p. and mixed m. p. 119° with an authentic specimen kindly provided by Dr. J. W. Cornforth. The infrared spectra of the two samples were identical (Found: C, 79·0; H, 7·6. Calc. for $C_{16}H_{18}O_2$: C, 79·3; H, 7·5%).

DEPARTMENT OF ORGANIC CHEMISTRY,
THE UNIVERSITY, LIVERPOOL.
[Present address: DEPARTMENT OF CHEMISTRY,
THE UNIVERSITY, IBADAN, NIGERIA.]

[*Received, November 15th,* 1957.]

---

## 246. N-*Oxides and Related Compounds. Part VIII.* The Electric Dipole Moments of a Series of* 4-*Substituted Pyridine–Boron Trichloride Complexes.*

By C. M. BAX, A. R. KATRITZKY, and L. E. SUTTON.

The dipole moments of some compounds indicated in the title afford evidence that the pyridine–boron trichloride system can create a deficit of electrons in the 4-position, but (unlike the analogous 1-oxides) not an excess.

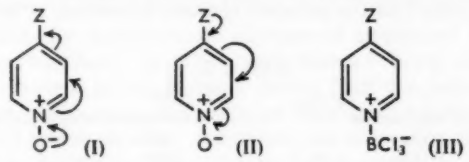
KATRITZKY, RANDALL, and SUTTON [1] have shown that the mesomeric moments of 4-substituted pyridine 1-oxides are always greater than those of the corresponding pyridines for both electron-withdrawing and electron-releasing substituents, and have suggested that this is because electron-shifts of both type (I) and type (II) can take place in appropriate pyridine 1-oxides.

Electron shift of type (I) occurs because there is a spare electron-pair on the oxygen

* Part VII, *J.*, 1958, 150.

[1] Katritzky, Randall, and Sutton, *J.*, 1957, 1769.

atom; therefore it should not occur in analogous compounds wherein the oxygen is replaced by an atom without such a spare electron-pair. In such compounds, the mesomeric moment should be larger for those with electron-releasing 4-substituents, but smaller for




those with electron-withdrawing 4-substituents, than the mesomeric moments of the corresponding 4-substituted pyridines. To test this prediction a series of 4-substituted pyridine–boron trichloride complexes (III) has now been prepared (Table 1), and their dipole moments have been measured.

TABLE 1. *Substituted pyridine–boron trichloride complexes.*

| No. | 4-Subst. | Yield (%) [a] | M. p. | Crystal form | Solvent for recrystn. |
|---|---|---|---|---|---|
| 1 | OMe | 63 | 91—93° | Needles [b] | EtOH |
| 2 | Cl | 79 | 167·5—169 | Needles | MeOH |
| 3 | Me | 77 | 126·5—127·5 | Needles | EtOH |
| 4 | H | 70 | 113—114 [a] | Plates | EtOH |
| 5 | $CO_2Et$ | 70 | 110—111 | Plates | EtOH |
| 6 | CN | 85 | 149—150·5 | Prisms | MeOH |

| | | Found (%) | | | | Required (%) | | | |
|---|---|---|---|---|---|---|---|---|---|
| No. | Formula | C | H | N | Cl | C | H | N | Cl |
| 1 | $C_6H_7ONBCl_3$ | 31·9 | 3·3 | 6·0 | 46·4 | 31·8 | 3·1 | 6·2 | 47·0 |
| 2 | $C_5H_4NBCl_4$ | 26·3 | 2·1 | 5·8 | 61·0 | 26·0 | 1·8 | 6·1 | 61·4 |
| 3 | $C_6H_7NBCl_3$ | 34·2 | 3·4 | 6·2 | — | 34·3 | 3·4 | 6·7 | — |
| 5 | $C_9H_9O_2NBCl_3$ | 35·9 | 3·7 | 4·7 | 39·6 | 35·8 | 3·4 | 5·2 | 39·6 |
| 6 | $C_6H_4N_2BCl_3$ | 32·5 | 2·0 | 12·3 | 48·8 | 32·5 | 1·8 | 12·7 | 48·1 |

[a] Gerrard and Lappert, *J.*, 1951, 1020, give m. p. 114·5—115°. [b] Deliquescent.
[c] Prepared in light petroleum, except that no. 6 was prepared in light petroleum–benzene.

## EXPERIMENTAL

*Preparation of Compounds.*—4-Nitro-, 4-acetyl-, 4-dimethylamino-, and 4-ethoxycarbonylpyridine were prepared as stated in ref. 1. 4-Cyanopyridine was purchased.

4-Chloropyridine (45%), b. p. 46°/15 mm., was prepared from 4-nitropyridine 1-oxide by Ochiai and Suzuki's method [2] (yield 58·6%; b. p. 53—55°/20 mm.).

4-Picoline, b. p. 144°, was prepared by catalytic reduction of its 1-oxide.

4-Methoxypyridine 1-oxide (7·5 g.), iron filings (6 g.), and acetic acid (30 c.c.) were kept for 4 hr. at 100°, then basified with 30% aqueous sodium hydroxide and filtered (sintered glass). The solid was washed and the solution extracted with ether. 4-Methoxypyridine (4 g., 63%), b. p. 188·5—189·5° (lit.,[3] b. p. 190°), was recovered from the dried ($MgSO_4$) extracts.

4-Cyanopyridine 1-oxide [4] had m. p. 222·5—224·5° (lit.,[4] m. p. 220—221°).

*Preparation of Pyridine–Boron Trichloride Complexes.*—Boron trichloride in light petroleum (b. p. 40—60°) (6 c.c. of 1·67N-solution) was added dropwise, with agitation, at 0°, to the pyridine (0·01 mole) in light petroleum (*ca.* 20 c.c.; for compound no. 6, sufficient benzene was added to bring it into solution). The adduct was filtered off and recrystallised by adding it rapidly to sufficient hot solvent, agitating the whole, and filtering it without delay into a precooled receiver. Some of the adducts decomposed very readily if the above recrystallisation procedure was not followed; even so it was not possible to purify the 4-nitro-, 4-dimethylamino-, and 4-acetyl adducts; the last gave apparently 4-*acetylpyridine hydrochloride*, plates, m. p. 150—154° (decomp.) (Found: C, 53·0; H, 5·2. $C_7H_8ONCl$ requires C, 53·3; H, 5·1%).

[2] Ochiai and Suzuki, *Pharm. Bull. Japan*, 1954, **2**, 247.
[3] Ochiai and Ishii, *J. Pharm. Soc. Japan*, 1951, **71**, 1092.
[4] Ochiai, *J. Org. Chem.*, 1953, **18**, 534.

XUM

*Physical Measurements.*—Electric dipole moments were determined by measuring the dielectric constants, specific volumes, and refractive indices (for $Na_D$ light) of benzene solutions at 25°, by the methods described by Everard and Sutton [5] for their small scale technique, with the heterodyne capacitance meter described by Hill and Sutton.[6] The meter was calibrated by assuming the value 2·2727 for the dielectric constant of benzene at 25°.[7] The pyknometer was calibrated with air-free distilled water. The refractive index difference, $\Delta n_D$, between the solution and benzene was measured with a Pulfrich refractometer.

The computation of moments, and the notation used here, follow the pattern set by Everard, Hill, and Sutton [8] so that no allowance has been made for atom polarisation except where specifically stated, other than that implicit in using $[R]_D$ as the distortion polarisation. For molecules of such high polarity as in the present series this is of negligible effect. In one case it was impossible to measure the refractive index, because the solute crystallised in the refractometer cell. Tables of atomic and molecular refractions were used to obtain $_EP$. The values used are given at the foot of Table 2.

TABLE 2.

Pyridine–boron trichloride

| $10^4W$ | $\varepsilon$ | $V$ | $10^5\Delta n_D$ |
|---|---|---|---|
| 1048 | 2·3069 | 1·1444 | 6 |
| 2140 | 2·3430 | 1·1436 | 12 |
| 3756 | 2·3955 | 1·1429 | 19 |
| 4763 | 2·4299 | 1·1424 | 29 |

$\varepsilon = 2·2725 + 32·94W$; $V = 1·1447 - 0·467W$; $\Delta n_D = 0·059W$; $_EP = 45·7$ c.c.; $_TP = 1257·0$ c.c.; $\mu = 7·70 \pm 0·02$ D

4-Chloropyridine–boron trichloride

| $10^4W$ | $\varepsilon$ | $V$ | $10^5\Delta n_D$ |
|---|---|---|---|
| 1013 | 2·2945 | 1·1441 | 5 |
| 1942 | 2·3142 | 1·1434 | 11 |
| 2116 | 2·3171 | 1·1434 | 11 |
| 3360 | 2·3446 | 1·1425 | 14 |

$\varepsilon = 2·2726 + 21·33W$; $V = 1·1447 - 0·63W$; $\Delta n_D = 0·00001 + 0·043W$; $_EP = 40·51$ c.c.; $_TP = 960·9$ c.c.; $\mu = 6·71 \pm 0·03$ D

4-Methoxypyridine–boron trichloride

| $10^4W$ | $\varepsilon$ | $V$ | $10^5\Delta n_D$ |
|---|---|---|---|
| 1044 | 2·3130 | 1·1441 | 8 |
| 1673 | 2·3373 | 1·1438 | 6 |
| 2324 | 2·3614 | 1·1432 | 12 |
| 2976 | 2·3860 | 1·1430 | 13 |
| 3714 | 2·4135 | — | 21 |

$\varepsilon = 2·2733 + 37·88W$; $V = 1·1446 - 0·563W$; $\Delta n_D = 0·051W$; $_EP = 45·2$ c.c.; $_TP = 1651·5$ c.c.; $\mu = 8·86 \pm 0·02$ D

4-Ethoxycarbonylpyridine–boron trichloride

| $10^4W$ | $\varepsilon$ | $V$ | $10^5\Delta n_D$ |
|---|---|---|---|
| 995 | 2·2967 | 1·1445 | 4 |
| 1240 | 2·3019 | 1·1444 | 5 |
| 1837 | 2·3167 | 1·1440 | 8 |
| 2173 | 2·3261 | 1·1438 | 7 |

$\varepsilon = 2·2722 + 24·38W$; $V = 1·1448 - 0·44W$; $\Delta n_D = 0·034W$; $_EP = 60·7$ c.c.; $_TP = 1287·6$ c.c.; $\mu = 7·74 \pm 0·07$ D

4-Methylpyridine–boron trichloride

| $10^4W$ | $\varepsilon$ | $V$ | $10^5\Delta n_D$ |
|---|---|---|---|
| 1110 | 2·3157 | 1·1441 | 5 |
| 1549 | 2·3325 | 1·1438 | 6 |
| 1858 | 2·3406 | 1·1435 | 10 |
| 3264 | 2·3928 | 1·1430 | 13 |
| 3715 | 2·4104 | 1·1427 | 17 |

$\varepsilon = 2·2738 + 36·69W$; $V = 1·1446 - 0·506W$; $\Delta n_D = 0·044W$; $_EP = 44·3$ c.c.; $_TP = 1477·3$ c.c.; $\mu = 8·37 \pm 0·06$ D

4-Cyanopyridine–boron trichloride

| $10^4W$ | $\varepsilon$ | $V$ | $10^5\Delta n_D$ |
|---|---|---|---|
| 694 | 2·2783 | 1·1442 | — |
| 1176 | 2·2827 | 1·1441 | — |
| 1510 | 2·2859 | 1·1439 | — |
| 2053 | 2·2906 | 1·1435 | — |

$\varepsilon = 2·2725 + 8·79W$; $V = 1·1447 - 0·508W$; $_EP = 47·2$ c.c.;[a] $_TP = 407·8$ c.c.; $\mu = 4·20 \pm 0·05$ D

4-Cyanopyridine 1-oxide

| $10^4W$ | $\varepsilon$ | $V$ | $10^5\Delta n_D$ |
|---|---|---|---|
| 318 | 2·2731 | 1·1443 | 5 |
| 483 | 2·2734 | 1·1444 | 2 |
| 494 | 2·2733 | 1·1444 | 2 |
| 570 | 2·2737 | 1·1443 | 6 |

$\varepsilon = 2·2726 + 1·56W$; $V = 1·1446 - 0·427W$; $\Delta n_D = 0·063W$; $_EP = 30·31$ c.c.; $_TP = 58·9$ c.c.; $\mu = 1·22 \pm 0·13$ D

[a] It was impossible to measure refractive indices because the solute crystallised in the refractometer cell. The following values were used to obtain $_EP$: pyridine = 24·07 c.c.; H = 1·10 c.c.; CN = 5·54 c.c. (Landolt–Börnstein Tabellen) and $BCl_3 = 18$ c.c. (Phillips, Hunter, and Sutton *J.*, 1945, 146).

[5] Everard and Sutton, *J.*, 1951, 16.
[6] Hill and Sutton, *J.*, 1953, 1482.
[7] Hartshorn and Oliver, *Proc. Roy. Soc.*, 1929, *A*, **123**, 664.
[8] Everard, Hill, and Sutton, *Trans. Faraday Soc.*, 1950, **46**, 417.

## Discussion

The mesomeric moment in a Z-substituted pyridine–boron trichloride complex may be defined as:

$$\mu_m(ZPyBCl_3) = \mu(ZPyBCl_3) + [\mu(PyBCl_3) - \mu(AlkZ)]$$

the analogous definitions for the mesomeric moments of substituted pyridines and pyridine 1-oxides adopted by Katritzky, Randall, and Sutton [1] being used. This mesomeric moment is therefore defined as the moment arising from the redistribution of electrons when Z is substituted into an aromatic system of some kind, relative to that which occurs when Z is substituted into a paraffin. As before,[1] in order that the mesomeric moment may be calculated it is assumed to have the same direction as in the corresponding benzene compound. The direction of the total moment can then be calculated. Table 3 gives the results together with other data taken from Katritzky *et al.*[1]

Table 3.

| | Pyridine–boron trichloride: gross moments | | Angle of mesomeric moment in substd. benzene [a] | Mesomeric moment magnitudes | | | | Vectorial difference of pyridine–$BCl_3$ and pyridine moments | |
|---|---|---|---|---|---|---|---|---|---|
| 4-Subst. | magnitude | angle | | Substd. benzene | 4-Substd. pyridines | 4-Substd. pyridine–$BCl_3$ | 4-Substd. pyridine 1-oxide | magnitude | angle |
| OMe | 8·86 ± 0·02 | 6° | 12° | 0·96 | 1·16 | 1·35 | 1·39 | 6·06 | 1½° |
| Cl | 6·71 ± 0·03 | 0 | 0 | 0·41 | 0·57 | 1·02 | 0·59 | 5·93 | 0 |
| Me | 8·37 ± 0·06 | 0 | 0 | 0·35 | 0·39 | 0·67 | 0·50 | 5·76 | 0 |
| H | 7·70 ± 0·02 | — | — | — | — | — | — | 5·48 | 0 |
| $CO_2Et$ | 7·74 ± 0·07 | 13 | 180 | 0·50 | 0·47 | 0·17 | 0·93 | 5·75 | ½ |
| CN | 4·20 ± 0·05 | 0 | 180 | 0·45 | 0·27 | 0·10 | 1·5 [b] | 5·85 | 0 |

[a] We define the gross and the mesomeric moment angles as in ref. 1, *i.e.*, if the moment acts along the Z–C bond, Z being the positive end of the dipole, then it has angle 0°. [b] $_TP - _EP = 30·3$ c.c. ($_AP$ being neglected), if $_AP = 11·9$ c.c. (Finn, Hampson, and Sutton, *J.*, 1938, 1254, give $_AP = 11·9$ c.c. for *p*-dicyanobenzene), then $_oP = 18·4$ c.c. and $\mu = 0·95$ D. This resultant moment may be at either 0° or 180° (see footnote *a*). The mesomeric moments calculated for these two alternatives are 0·3 D at 0 and 1·5 at 180°. In all known cases, the $C\equiv N$ group is electron-attracting. We therefore take the latter value as more reasonable. This provides another example where the mesomeric moment of a pyridine 1-oxide with an electron-attracting 4-substituent is greater than that of the corresponding pyridine.[1]

It is seen that for the electron-releasing substituents OMe, Cl, and Me the mesomeric moments in the pyridine–boron trichloride complexes are greater than, but for the electron-accepting substituents $CO_2Et$ and CN are smaller than, those in the corresponding pyridines. Somewhat surprisingly, the 1-oxide with a 4-chloro-substituent does not show a corresponding large increase of mesomeric moment relative to the pyridine. As was pointed out in the previous paper, this can be attributed to the power of the $^+N{-}O^-$ group to donate electrons to the ring when required. The dual behaviour of the chlorine atom, which can attract electrons or release them according to circumstances, is shown particularly clearly in this case.

An alternative way of using the dipole-moment data is to consider the vectorial difference between the moments of the pyridine–boron trichloride complexes and those of the substituted pyridines, giving the increase in total moment due to the co-ordination of the $BCl_3$ group. This is greater for all the substituted compounds than for the parent one, because (*a*) electron-releasing substituents release more into the pyridine–boron trichloride system than into the pyridine system and (*b*) electron-withdrawing groups take less out.

These results support the view [1] that the pyridine 1-oxide system can produce either an excess or a deficit of electrons at the 4-position as required by the substituent there. Independent infrared evidence of this effect has now been obtained and will be published as a separate paper.

This investigation was carried out during the tenure (by A. R. K.) of an I.C.I. Fellowship.

The Physical Chemistry and the Dyson Perrins Laboratory,
The University, Oxford.

[*Received, July 3rd,* 1957.]

XUM

## 247. *N-Oxides and Related Compounds. Part IX.* The Electric Dipole Moments of Pyridine- and Trimethylamine-Boron Trihydride and Trihalide Complexes.*

By C. M. Bax, A. R. Katritzky, and L. E. Sutton.

The mesomeric moments in pyridine–boron trihydride and trihalide complexes are large, negative, and approximately constant. From these and the positive mesomeric moment in pyridine 1-oxide, the moment due to the inward drift of electrons from the oxygen atom can be estimated.

The variation of moment change due to complex formation by both trimethylamine and pyridine is in the order: $BF_3 < BH_3 \leqslant BCl_3 < BBr_3$. The reasons for this are discussed.

In the preceding paper, the mesomeric moments for 4-substitution into the pyridine–boron trichloride complex were measured and compared with those for 4-substitution into pyridine and pyridine 1-oxide. Such complexes are interesting for other reasons, and some of these are pursued in this paper. In particular, the mesomeric moments in the aromatic system for attachment of the acceptor molecules are derived, and the magnitudes of the moments due to formation of complexes involving trimethylamine or pyridine are estimated when the acceptor molecules are boron trihydride, trifluoride, trichloride, and tribromide.

### Experimental

*Trimethylamine–Borane.*—The following simplification of Schaeffer and Anderson's method [1] was convenient: aqueous trimethylamine (25—30%; 10 c.c.) and concentrated hydrochloric acid (10 c.c.) were mixed and evaporated at 100°/13 mm. for 30 min. after solidification had taken place. Then a slurry of lithium borohydride (0·84 g.) in ether (150 c.c.) which had been refluxed for 30 min. was added. The whole was refluxed for 30 min., filtered, and evaporated to give the adduct (1·5 g., 60%), m. p. 92—93° (lit.,[1] yield 85%, m. p. 93°). The compound was purified by sublimation.

*Pyridine–Borane.*—This was prepared as described in ref. 2 and distilled. The compound is evidently subject to superheating for at constant pressure (0·15 mm.) six fractions were collected: the b. p. rose from 58° to 78° for the third fraction, and fell to 68° again; $n_D^{20}$ was 1·5315 for the first fraction and 1·5310 for all of the others [ref. 2 gives $n_D^{25}$ 1·5280; ref. 3 gives v. p. (mm.) 0·1 at 25°, 0·15 at 45°, 0·35 at 60°, 0·9 at 85°, 1·8 at 99°; the increase in pressure seems unduly small for the temperature range quoted].

*Pyridine–Boron Trifluoride.*—This was prepared as in ref. 4. It sublimed at 100°/0·15 mm. and then had m. p. 46—47° (lit.,[4,5] m. p. 45°, 47—48°). It was not possible to recrystallise it from ethyl alcohol.

*Trimethylamine–Boron Tribromide.*—To 25—30% (w/v) aqueous trimethylamine (25 c.c.), benzene (25 c.c.), and light petroleum (b. p. 40—60°; 25 c.c.) was added sodium hydroxide (25 g.). After 10 min. the organic layer was separated and dried (NaOH). Boron tribromide (25 c.c. of 0·5M-solution in light petroleum) was added slowly with cooling in solid carbon dioxide–ethanol. The *adduct* (3·1 g., 80%), crystallised five times from ethanol, formed needles, m. p. 230—232° (Found: C, 11·8; H, 2·7; N, 4·2; Br, 77·2. $C_3H_9NBBr_3$ requires C, 11·6; H, 2·9; N, 4·5; Br, 77·4%]. Only an abortive attempt to prepare this compound has been previously recorded.[6]

*Pyridine–Boron Tribromide.*—Boron tribromide (10 c.c. of 0·5M-solution in light petroleum) was added in 5 min. to pyridine (0·5 c.c.) in light petroleum (10 c.c.) with cooling as above.

* Part VIII, preceding paper.

[1] Schaeffer and Anderson, *J. Amer. Chem. Soc.*, 1949, **71**, 2143.
[2] Taylor, Grant, and Sands, *ibid.*, 1955, **77**, 1506.
[3] Brown, Schlesinger, and Cardon, *ibid.*, 1942, **64**, 325.
[4] van der Meulen and Heller, *ibid.*, 1932, **54**, 4404.
[5] Brown and Holmes, *ibid.*, 1956, **78**, 2174.
[6] Johnson, *J. Phys. Chem.*, 1912, **16**, 1.

The adduct (1·35 g., 80%), twice recrystallised from ethanol, had m. p. 127—128° not raised by further recrystallisation (Found: C, 18·3; H, 1·6; N, 4·1. Calc. for $C_5H_5NBBr_3$: C, 18·2; H, 1·5; N, 4·2%) (ref. 5 reports m. p. 128—129°; ref. 6 says that it becomes " brown and crispy " at 120°).

*Physical Measurements.*—For details see preceding paper. The results are recorded in Table 1.

TABLE 1.

*Pyridine–borane*

| $10^6W$ | $\varepsilon$ | $V$ | $10^5\Delta n_D$ |
|---|---|---|---|
| 3959 | 2·4315 | 1·1443 | 19 |
| 5577 | 2·4967 | 1·1441 | 30 |
| 7328 | 2·5678 | 1·1438 | 37 |
| 9504 | 2·6563 | 1·1437 | 46 |

$\varepsilon = 2{\cdot}2722 + 40{\cdot}35W$; $V = 1{\cdot}1446 - 0{\cdot}10W$; $\Delta n_D = 0{\cdot}00001 + 0{\cdot}05W$; $_TP = 734{\cdot}1$ c.c. $_EP = 30{\cdot}1$ c.c. $\mu = 5{\cdot}86 \pm 0{\cdot}01$ D

*Pyridine–boron trifluoride*

| $10^6W$ | $\varepsilon$ | $V$ | $10^5\Delta n_D$ |
|---|---|---|---|
| 1230 | 2·3179 | 1·1443 | — |
| 1997 | 2·3438 | 1·1438 | — |
| 2191 | 2·3499 | 1·1438 | — |
| 2771 | 2·3696 | 1·1436 | — |

$\varepsilon = 2{\cdot}2736 + 34{\cdot}94W$; $V = 1{\cdot}1446 - 0{\cdot}38W$; $_TP = 999{\cdot}0$ c.c. $_EP = 26{\cdot}8$ c.c.[a] $\mu = 6{\cdot}90 \pm 0{\cdot}05$ D

*Trimethylamine–borane*

| | | | |
|---|---|---|---|
| 2523 | 2·3520 | 1·1451 | −28 |
| 5596 | 2·4490 | 1·1461 | −62 |
| 6227 | 2·4681 | 1·1459 | −68 |
| 7920 | 2·5218 | 1·1465 | −85 |

$\varepsilon = 2{\cdot}2727 + 31{\cdot}45W$; $V = 1{\cdot}1445 + 0{\cdot}24W$; $\Delta n_D = -0{\cdot}11W$; $_TP = 461{\cdot}6$ c.c.; $_EP = 25{\cdot}1$ c.c. $\mu = 4{\cdot}62 \pm 0{\cdot}01$ D

*Pyridine–boron tribromide*

| | | | |
|---|---|---|---|
| 1665 | 2·3070 | 1·1433 | 9 |
| 1831 | 2·3125 | 1·1433 | 11 |
| 2619 | 2·3288 | 1·1428 | 15 |
| 4365 | 2·3629 | 1·1414 | 23 |

$\varepsilon = 2{\cdot}2734 + 20{\cdot}72W$; $V = 1{\cdot}1446 - 0{\cdot}73W$; $\Delta n_D = 0{\cdot}05W$; $_TP = 1322{\cdot}9$ c.c. $_EP = 50{\cdot}5$ c.c. $\mu = 7{\cdot}90 \pm 0{\cdot}06$ D

*Trimethylamine–boron tribromide*

| | | | |
|---|---|---|---|
| 2146 | 2·3058 | 1·1432 | 10 |
| 2794 | 2·3155 | 1·1428 | 13 |
| 3274 | 2·3228 | 1·1425 | 22 |

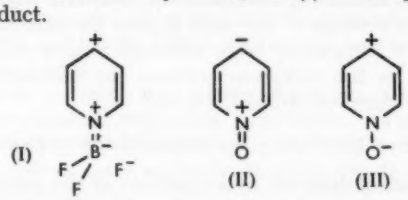
$\varepsilon = 2{\cdot}2728 + 15{\cdot}31W$; $V = 1{\cdot}1446 - 0{\cdot}64W$; $\Delta n_D = -0{\cdot}00001 + 0{\cdot}06W$; $_TP = 938{\cdot}3$ c.c. $_EP = 56{\cdot}2$ c.c. $\mu = 6{\cdot}57 \pm 0{\cdot}01$ D

[a] It was impossible to measure refractive indices because the solute crystallised in the refractometer cell. The following values were used to obtain $_EP$: $R_D$ (pyridine) = 24·07 c.c. (Landolt–Börnstein Tabellen) and $R_D(BF_3) = 2{\cdot}7$ c.c. (Phillips, Hunter, and Sutton, *J.*, 1945, 146).

## DISCUSSION

As in previous treatments, the algebraic difference of electric dipole moment between a pyridine complex and a trimethylamine complex may be taken as an approximate value for the contribution to the former moment of electron drifts induced by the highly polar dative link which joins the pyridine to the acceptor molecule. This statement assumes that the moments of the dative link and of the co-ordinated acceptor molecule are the same in the aromatic and the aliphatic compounds, which cannot be entirely true; but the errors which arise are probably small.

These differences appear in column 4 of Table 2 and show interesting features: for the boron compounds as adducts, the differences are all (*a*) roughly constant, (*b*) less than the difference between pyridine and trimethylamine, and (*c*) in the opposite sense from that of the oxygen atom as adduct.




(*a*) This observation indicates that the polarising power of the dative link plus co-ordinated adduct are much the same in all four cases, although the gross moments of the compounds increase by 35—40% in the series $BH_3$, $BF_3$, $BCl_3$, $BBr_3$. It is likely that the

polarisation is almost wholly an inductive effect in the aromatic ring, for canonical structures such as (I) are probably unimportant. This may be contrasted with the varying effect that the corresponding $CX_3$ groups have when attached to benzene, as shown by the differences between $C_6H_5{\cdot}CX_3$ and $CH_3{\cdot}CX_3$ in column 8. These indicate that the $CF_3$

TABLE 2.

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|
| Adduct for cols. 2 and 3 | $NMe_3$ adduct | Pyridine adduct | Pyridine adduct *less* $NMe_3$ adduct | Subst. for cols. 6 and 7 | Substd. methane | Substd. benzene | Substd. benzene *less* substd. methane | $NMe_3$ adduct *less* substd. methane | Pyridine adduct *less* substd. benzene |
| Nil | −0·65 [a] ±0·03 | −2·22 [b] ±0·02 | −1·57 | — | — | — | — | — | — |
| O | −5·02 [c] ±0·02 | −4·24 [c] ±0·02 | +0·78 | — | — | — | — | — | — |
| $BH_3$ | −4·62 [d] ±0·01 | −5·86 [d] ±0·01 | −1·24 | $CH_3$ | 0 | +0·40 | +0·40 | −4·62 | −6·26 |
| $BF_3$ | −5·63 [e] ±0·03 | −6·90 [d] ±0·05 | −1·27 | $CF_3$ | −2·34 [g] | −2·56 [h] | −0·22 | −3·29 | −4·34 |
| $BCl_3$ | −6·31 [e] ±0·03 | −7·70 [d] ±0·02 | −1·39 | $CCl_3$ | −1·59 [j] ±0·01 | −2·02 [j] ±0·01 | −0·43 | −4·72 | −5·68 |
| $BBr_3$ | −6·57 [d] ±0·01 | −7·90 [d] ±0·06 | −1·33 | $CBr_3$ | Not available | | — | — | — |

A positive sign means that the positive pole of the dipole is towards the adduct or the corresponding group. [a] Groves and Sugden's figures recalculated (*J.*, 1937, 1779). [b] Curran and Leis's figures recalculated (*J. Amer. Chem. Soc.*, 1945, **67**, 79). [c] Linton's figures recalculated (*ibid.*, 1940, **62**, 1945). [d] Present investigation. [e] Philips, Hunter, and Sutton's figures recalculated, neglecting ${}_AP$ (*J.*, 1945, 146). [f] Selected from data in Wesson's tables (Wesson, "Tables of Electric Dipole Moment," The Technology Press, Massachusetts Institute of Technology, Cambridge, Mass. U.S.A., 1948). [g] Fuoss's value (*J. Amer. Chem. Soc.*, 1938, **60**, 1633) recalculated by Conradi and Li (*ibid.*, 1953, **75**, 1785). [h] Frieser, Hobbs, and Gross (*ibid.*, 1949, **71**, 111). [j] Sutton's figures recalculated (*Proc. Roy. Soc.*, 1931, *A*, **133**, 668); see also ref. *h* for a value for benzotrichloride.

group is less effective than the $CCl_3$ in polarising; but it must be emphasised that the value for $CH_3{\cdot}CF_3$ is a vapour-phase determination which may not be strictly comparable with the other values which are for benzene solutions. This point will be taken up below.

(*b*) This decrease is not what would at first be expected, because the polarisation of the aromatic system by the dative link and the adduct molecule ought to be greater than that due to the polarity within the pyridine ring. The differences are not, however, truly comparable; for in the trimethylamine complexes the bonding orbitals of the nitrogen atom used in the N–C bonds have more *s* character than have those in trimethylamine itself. If hybridisation in the latter could be changed to that in the former, the dipole moment of the lone pair, and hence of the whole molecule, would increase markedly; and the apparent mesomeric moment in pyridine would correspondingly decrease.

(*c*) The third observation again emphasises the great difference between the boron compounds and the oxygen atom as adducts, only the latter having unshared electrons which by delocalisation in a molecular π-orbital can drift into the ring. The algebraic difference between the two mesomeric moments, *viz.*, between +0·78 and −1·24 to −1·39, which is *ca.* 2·1 gives some measure of this drift against the polarising action of the $^+N{-}O^-$ bond in the 1-oxide. It is remarkably large, although smaller than the estimate of 2·35 D which Linton [7] obtained as the difference between the moment predicted for pyridine 1-oxide (6·59 D) and that observed (4·24 D), *i.e.*, as:

$$\Delta\mu = \mu(\text{pyridine oxide}) - \mu(\text{pyridine}) - [\mu(\text{trimethylamine oxide}) - \mu(\text{trimethylamine})]$$

This implies that the effect of different hybridisations of the nitrogen atom in trimethylamine and its oxide can be ignored, which, as has been emphasised above, is probably untrue. The larger the moment taken for trimethylamine, the smaller are both the

[7] Linton, *J. Amer. Chem. Soc.*, 1940, **62**, 1945.

predicted value and the difference. The present estimate, using only tetrahedrally hybridised aliphatic compounds, should avoid this difficulty.

Further, Linton's value should give the differential effect of contributions by structures (II) and (III) and was surprisingly large in view of chemical [8] and dipole-moment [9] evidence that forms (II) and (III) are of comparable importance. Our estimate should represent the moment due to the inward drift of electrons (II) only (within the limitations which apply to all comparisons between tetrahedrally and trigonally hybridised compounds), because the induced polarisation due to the external polar bond (cf. III) is present both in the complexes and in the *N*-oxide, and should cancel approximately in our calculation. This may be seen from the explicit statement:

$$\Delta'\mu = \mu(\text{pyridine 1-oxide}) - \mu(\text{trimethylamine oxide}) - [\mu(\text{pyridine boron complex}) - \mu(\text{trimethylamine boron complex})]$$

$^+N{-}B^-$ *Moment.*—The second main matter is that of the magnitude of the moment change due to co-ordination, and its connection with the nature of the X atom in the acceptor $BX_3$ molecule.

The most interesting quantity to evaluate would be the moment of the $^+N{-}B^-$ bond; but this is always difficult because of the contribution from the tetrahedrally hybridised $BX_3$ group, which cannot be directly observed. The simplest way of allowing for it is to compare the moments of the complexes with those of the $\geqslant C{-}CX_3$ compounds. The available differences are given in Table 2, for aliphatic pairs in column 9 and for aromatic ones in column 10.

In the aromatic series they are complicated by the changes in mesomeric moment, especially for the case of X = H. In the aliphatic series, there is the possible incompatibility of the moment for $CH_3{\cdot}CF_3$, from vapour measurements, with the others which are all from solution measurements. Nevertheless, both series show that the differences are roughly the same for X = H and for X = Cl, but are less for X = F. Subtraction of the moments of $HCX_3$ compounds from those of either the pyridine or the trimethylamine complexes, as is shown in Table 3, gives differences that increase in the order F, H, Cl, Br. Acceptor power, therefore, appears to be in the order:

$$BF_3 < BH_3 \leqslant BCl_3 < BBr_3$$

For the halides, this is qualitatively the same as that found by H. C. Brown and Holmes [5] from the heats of formation of the complexes.

TABLE 3.

| X | $\mu(Me_3N{-}BX_3)$ | $\mu(CHX_3)$ | $\mu(Me_3N{-}BX_3) - \mu(CHX_3)$ | $\mu(C_5H_5N{-}BX_3)$ | $\mu(C_5H_5N{-}BX_3) - \mu(CHX_3)$ |
|---|---|---|---|---|---|
| H | 4·62 | 0 | 4·62 | 5·86 | 5·86 |
| F | 5·63 | 1·59 | 4·04 | 6·90 | 5·31 |
| Cl | 6·31 | 1·18 | 5·13 | 7·70 | 6·52 |
| Br | 6·57 | 1·0 | 5·57 | 7·90 | 6·90 |

Acceptor power can be regarded as being due to the possession by the boron atom of an unfilled, low-lying orbital, and to any formal positive charge which the atom bears because of the polarity of the B–X links.

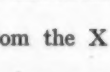
It can hardly be given a precise and general definition, because different methods of assessing it would require different definitions. In relation to the thermodynamic stability of the complex, there would, for example, certainly have to be reference to the steric effects between donor and acceptor molecules,[10] which effects, however, may not enter,

[8] Katritzky, *Quart. Rev.*, 1956, **10**, 395.
[9] Katritzky, Randall, and Sutton, *J.*, 1957, 1769; see also preceding paper.
[10] *Inter al.*, Brown and Nakagawa, *ibid.*, p. 2197; Brown and Barbaras, *ibid.*, 1947, **69**, 1137; Brown and Taylor, *ibid.*, p. 1332; Brown and Horowitz, *ibid.*, 1955, **77**, 1733.

XUM

at least not in the same way, into the definition from dipole-moment change. We need more information on this point. Exact parallels between estimates of acceptor power from different means of determination are therefore not to be expected; but qualitative agreement is probably significant.

Two explanations may be offered for the order observed from dipole-moment changes:

(*a*) Back-co-ordination from the X atoms, involving structures of type  with π-bonds, will reduce the net formal positive charge and also saturate the spare orbital. Decrease of back-co-ordination in the order $BF_3 > BCl_3 > BBr_3$ would then explain the acceptor order observed for the halides. The relative position of the $BH_3$ complex could hardly be predicted; but it may be noted that, although the low polarity of the B–H bonds may give little positive charge to the boron atoms, there is no back-co-ordination at all.

(*b*) From simple electrostatic considerations, it can be seen that, although the formal positive charge on the B atom attracts lone-pair electrons, the negative ones on the X atoms repel them. Hence, for a given formal charge on the B and the X atoms, the repulsion would decrease as the B–X distance increases, and so the acceptor power might increase in the observed order. Again, the relative position of the $BH_3$ complex could hardly be predicted, but neither positive nor negative formal charges would be large.

The bond lengths in the free halides are all less than would be predicted by the simple addition of covalent radii: B–F is 19%, B–Cl is 6·9%, and B–Br is 7·4% less. This indicates that back-co-ordination is much greater in the first than in the other two where it is roughly the same.

It is likely that both explanations have partial validity.

[*Note Added January 20th*, 1958.—In a personal communication, Dr. N. N. Greenwood and his colleagues have informed us of recent results on the electrical conductivity of the molten pyridine–boron trichloride complex. These show that there is about 1% dissociation into kinetically free ions which are thought to be $[Py_2BCl_2]^+$ and $[BCl_4]^-$. If this substance retains the ionic dimerised form in dilute solution in benzene, our conclusions from the electric polarisation measurements would need drastic revision. It is probable, *a priori*, that the equilibrium form would be different, because the much smaller concentration of the benzene solutions used would not favour dimerization; and the lower dielectric constant would not favour an even more highly polar form (μ probably 10—15 D) than the simple monomer. If there were an equilibrium between these two forms over the range of weight fraction used (0·001—0·005), it would be expected that the proportions would change and that the $\epsilon/w_2$ curve would not be the normal rectilinear one but would show a positive curvature. In fact, the departures from rectilinearity are within the known experimental error generally found, *viz.*,

| $10^6 w_2$ | 0 | 1048 | 2140 | 3756 | 4763 |
|---|---|---|---|---|---|
| Δ | +0·0002 | −0·0001 | −0·0001 | −0·0008 | +0·0004 |

They show negligible curvature. There is therefore no indication of a change of solute form.

Measurements of molar electrical conductivity in benzene solution made by Mr. E. W. Randall (*ca.* $10^{-6}$ cm.$^2$ ohm$^{-1}$ mole$^{-1}$) combined with the analysis used by N. N. Greenwood and K. Wade (*J.*, in the press) for pyridine complexes with gallium trichloride, indicate that the solute is dissociated into kinetically free ions only to the extent of about 1 part in $10^8$. Therefore if it were in the suggested ionic form it would be effectively dimeric. Measurements of molecular weight in benzene by the Beckmann method, made by Mr. M. Hely Hutchinson, give a value of 186 ± 30 (twice standard deviation) which is sufficient proof that the substance is monomeric (*M*, 197) and not dimeric.

These results confirm that the form assumed for the solution, *viz.*, $Py,BCl_3$, is correct in our solutions.]

We thank Borax Consolidated, Ltd., for a generous grant of boron tribromide and Mr. E. W. Randall and Mr. M. Hely Hutchinson for making the measurements referred to in the added *Note*. This investigation was carried out during the tenure (by A. R. K.) of an I.C.I. Fellowship.

DYSON PERRINS LABORATORY AND PHYSICAL CHEMISTRY LABORATORY,
THE UNIVERSITY, OXFORD. [*Received, September 11th*, 1957.]

---

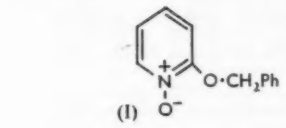
## 248. N-*Oxides and Related Compounds.*[1] *Part X.** *The Hydrogenation of Some Pyridine 1-Oxides.*

By A. R. KATRITZKY and A. M. MONRO.

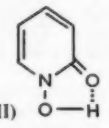
3- and 4-Substituted pyridine 1-oxides are smoothly hydrogenated to pyridines over palladium; 2-substituents somewhat hinder the reduction. Carbon–carbon double bonds and chlorine tend to be reduced before an *N*-oxide group. The rate of reduction of such substituents is not very different from the rate in the corresponding pyridine.

MANY individual observations, but no systematic investigation, of the catalytic hydrogenation of pyridine 1-oxides containing other reducible groups have been made. Ochiai [2] emphasised the comparative resistance to reduction of aromatic *N*-oxides. Indeed other groups have often been selectively reduced, but in other work 1-oxide functions were lost.

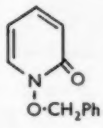
Shaw [3] debenzylated 2- and 4-benzyloxypyridine 1-oxide (cf. I) to 1-hydroxy-2- and -4-pyridone (cf. II) (see ref. 4 for further examples), and the isomeric compound (III) behaved similarly.[5] However, the 4-isomer of (I) has also given 4-pyridone; [6] 4-methoxy-, 4-ethoxy-, and 4-phenoxy-pyridine 1-oxides over palladium [7] or nickel [8] gave the alkoxy-pyridine (also true in quinoline series [9]), and 4-hydroxy-1-oxides gave 4-pyridone and 4-quinolone.[8,9]



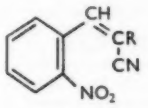
(I)



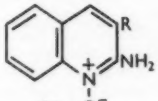
(II)



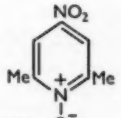
(III)



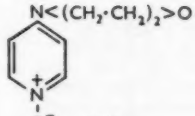
(IV)



(V)



(VI)



(VII)

The nitro-cyanides (IV; R = Ph or $CO_2Et$) were hydrogenated [10] to aminoquinoline 1-oxides (V), implying resistance of the latter to reduction. 4-Nitro-pyridine and -quinoline

* Part IX, preceding paper.

[1] For general review see Katritzky, *Quart. Rev.*, 1956, **10**, 395.
[2] Ochiai, *J. Org. Chem.*, 1953, **18**, 534.
[3] Shaw, *J. Amer. Chem. Soc.*, 1949, **71**, 67.
[4] Lott and Shaw, *ibid.*, p. 70.
[5] Part V, Gardner and Katritzky, *J.*, 1957, 4375.
[6] Ochiai, Teshigawa, Oda, and Naito, *J. Pharm. Soc. Japan*, 1945, **65**, 5/6*A*, 1; *Chem. Abs.*, 1951, **45**, 8527.
[7] Ochiai and Katada, *J. Pharm. Soc. Japan*, 1943, **63**, 265; *Chem. Abs.*, 1951, **45**, 5152.
[8] Ishii, *J. Pharm. Soc. Japan*, 1951, **71**, 1092; *Chem. Abs.*, 1952, **46**, 5046.
[9] Ishii, *J. Pharm. Soc. Japan*, 1952, **72**, 1317; *Chem. Abs.*, 1953, **47**, 12, 386.
[10] Bauer, *Ber.*, 1938, **71**, 2226.

XUM

| No. | Pyridine reduced [a] | Condns.[b] | $H_2$ (mols.) | Time (hr.) | Pyridine obtained [a] | Yield (%) | How isolated [c] and m. p. | M. p. in lit. | Ref. | Analysis |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 1-O | S | 1 | 1·5 | — | 84 | P 162—163° M | 165—166° | *d* | — |
| 2 | 4-Me, 1-O | S | 1 | 2 | 4-Me | 82 | P 165 M | 166—167 | *e* | — |
| 3 | 2-Me, 1-O | S | 1 | 6 | 2-Me | 73 | P 163—164 M | 163 | *f* | — |
| 4 | 4-Ph, 1-O | S | 1 | 40 | 4-Ph | 89 | P 194 | 195—196 | *g* | *h* |
| 5 | 2-Ph, 1-O | S | 1 | 10 | 2-Ph | 87 | P 172—174 M | 175—176 | *g* | — |
| 6 | 2-$CH_2$Ph, 1-O | S | 1 | 22 | 2-$CH_2$Ph | 84 | P 139 M | 139—140 | *j* | — |
| 7 | 4-$NH_2$, 1-O | S | 1 | 4 | 4-$NH_2$ | 77 | 156—158 M | 158 | *k* | — |
| 8 | 2-$NH_2$, 1-O | S | 1 | 70 | 2-$NH_2$ | 85 | L 269 [i] M | 269—271 | *m* | — |
| 9 | 4-OMe, 1-O | S | 1 | 0·8 | 4-OMe | 92 | P 171—172 M | 171—172 | *n* | — |
| 10 | 4-$CH_2$·$CH_2$·CO·$NH_2$, 1-O | T | 1 | 6 | 4-$CH_2$·$CH_2$·CO·$NH_2$ | 88 | 163—165 M | 165—166 | *o* | — |
| 11 | 4-CO·NH·$CH_2$Ph, 1-O | T | 1 | *ca.* 6 | 4-CO·NH·$CH_2$Ph | 86 | 89—91 M | 90—92 | *p* | — |
| 12 | 4-$CO_2$Et, 1-O | S | 1 | 2·2 | 4-$CO_2$Et | 58 | P 124—125 M [q] | 147 | *r* | *s* |
| 13 | 4-$CO_2$Et, 1-O | S | 4 | 60 | " | 70 | P 172—174 | 172 | *u* | *v* |
| 14 | 3-$CO_2$Et, 1-O | S | 1 | 1 | 3-$CO_2$Et | 60 | P 144 M | 147·5—148 | *w* | — |
| 15 | 4-OH, 1-O | S | 1 | 3 | 4-OH | 85 | P 236 M [s] | 238—239 | *y* | — |
| 16 | 4-CH:CH·$CO_2$Et, 1-O | S | 1 | 2 | 4-$CH_2$·$CH_2$·$CO_2$Et, 1-O | 60 [t] | A 225—226 M | 227·5 | *p* | — |
| 17 | " " | T | 2 | 5·5 | 4-$CH_2$·$CH_2$·$CO_2$Et | 75 | A 162—165 M | 165—166 | *o* | — |
| 18 | 4-CH:CH·$CO_2$Et | S | 1 | 2 | 4-$CH_2$·$CH_2$·$CO_2$Et | 88 | B. p. 122°/1·4 mm. | 133°/9 mm. | *o* | — |
| 19 | 3-CH:CH·$CO_2$Et, 1-O | S | 1 | 2 | 3-$CH_2$·$CH_2$·$CO_2$Et, 1-O | 42 [uu] | A 224 | — | — | *ab* |
| 20 | " " | S | 2 | 4·5 | 3-$CH_2$·$CH_2$·$CO_2$Et | 58 | P 78 [v] | 103—104 | *ac* | *ad* |
| 21 | 3-CH:CH·$CO_2$Et | S | 1 | 2 | " | 84 | B. p. 138—140°/5 mm.<br>P 78 M | 138—140°/3 mm.<br>78 | *ac*<br>*ae* | —<br>— |
| 22 | 4-CH:CH·CO·$NH_2$, 1-O | U | 1 | 1·2 | 4-$CH_2$·$CH_2$·CO·$NH_2$, 1-O | 77 | 225—227 M | 227 | *p* | — |
| 23 | " " | U | 2 | 6 | 4-$CH_2$·$CH_2$·CO·$NH_2$ | 83 | 162—164 M | 166—167 | *o* | — |
| 24 | 3-CH:CH·CO·$NH_2$, 1-O | U | 1 | 0·4 | 3-$CH_2$·$CH_2$·CO·$NH_2$, 1-O | 77 | 220—222 M | 224 | *af* | — |
| 25 | " " | U | 2 | 1·3 | 3-$CH_2$·$CH_2$·CO·$NH_2$ | 80 | 116—117 [v] M | 136 | *ac* | *ah* |
| 26 | 4-CH:CH·$CO_2$H, 1-O | V | 2 | 5 | 4-$CH_2$·$CH_2$·$CO_2$H | 15 | 224—227 M | 228—230 | *o* | — |
| 27 | 3-CH:CH·$CO_2$H, 1-O | V | 2 | 3·5 | 3-$CH_2$·$CH_2$·$CO_2$H | 63 | 154 | 157—158 | *ai* | *ai* |
| 28 | 4-CH:CHPh, 1-O | S | 1 | 2 | 4-$CH_2$·$CH_2$Ph, 1-O | 90 | 117 | — | — | *aj* |
| 29 | " " | S | 2 | 7·5 | 4-$CH_2$·$CH_2$Ph | 89 | 70 | 70—71 | *ag* | *ak* |
| 30 | 4-CH:CHPh | S | 1 | 3·5 | " | 77 | 69 [v] | 70—71 | *ag* | — |
| 31 | 2-CH:CHPh, 1-O | S | 1 | 2 | 2-$CH_2$·$CH_2$Ph, 1-O | 45 | 78—79 | — | — | *am* |
| 32 | 2-CH:CHPh | S | 1 | 4 | 2-$CH_2$·$CH_2$Ph | 84 | P 125 | 125—127 | *ag* | *an* |
| 33 | 4-Cl, 1-O | S | 1 | 0·25 | 1-O | 85 | L 179—182 M | 182—184 | *ao* | — |
| 34 | " | S[ap] | 2 | 2 | — | 16 | P 161—163 M | 165—166 | *d* | — |
| 35 | 4-Cl | S[ap] | 1 | 0·35 | — | 76 | P 162—164 M | 165—166 | *d* | — |
| 36 | 4-O·$CH_2$Ph, 1-O | S | 2 | 5·5 | 4-OH | 80 | P 236—237 | 238—239 | *y* | *aq* |
| 37 | 4-$NO_2$, 1-O | S[ar] | 4 | 3 | 4-$NH_2$ | 90 | 156—158 M | 158 | *k* | — |
| 38 | 4-COMe, 1-O | S | 1 | 0·7 | 4-COMe | 29 | P 126—128 M | 129—130 | *as* | — |
| 39 | 3-COMe, 1-O | S | 1 | 1·1 | 3-COMe | 70 | P 130 | 130 | *at* | *au* |

1-oxides have given the 4-amino-analogues with [1,11-13] and without [9,13-15] retention of the 1-oxide function. 4-Nitro-2 : 6-lutidine 1-oxide (VI) gave [12] the azo-1 : 1′-dioxide in hydrochloric acid, the amino-1-oxide in water, and the aminolutidine in acetic acid. 4-Morpholinopyridine 1-oxide (VII) was hydrogenated [16] to the corresponding pyridine.

The conditions varied largely in the above work. We reduced some pyridines and 1-oxides under uniform conditions (palladium, room temperature and pressure) to investigate: (i) the reduction of the 1-oxide group in compounds without another easily reducible group; (ii) the order and selectivity of reduction in 1-oxides with such another group; and (iii) the effect of the 1-oxide function on the ease of reduction of other groups. The results are recorded in the Table.

(i) Pyridine 1-oxide is readily hydrogenated to pyridine (No. 1). A variety of 4-substituted pyridine 1-oxides (nos. 2, 4, 7, 9—12, 15) with no reduction-sensitive groups gave the analogous pyridines at rates which bore no obvious relation to the character of the substituent, and, except for phenyl, differed by a factor of less than 10. The results for 3-ethoxycarbonyl- and 3-acetyl-pyridine 1-oxide (nos. 14 and 39) and the differences in the times of uptake of one and two mols. of hydrogen by β-3-pyridylacrylic ester (nos. 19 and 20) and the amide 1-oxide (nos. 24 and 25) indicate similar behaviour in the 3-series. 2-Substituted pyridine 1-oxides (nos. 3, 5, 6, 8), except the phenyl compound, are

[11] Berson and Cohen, *J. Org. Chem.*, 1955, **20**, 1461; Kato, Hamaguchi, and Oiwa, *Pharm. Bull. Japan*), 1956, **4**, 178.
[12] Kato and Hamaguchi, *Pharm. Bull.* (*Japan*), 1956, **4**, 174.
[13] Naito, *J. Pharm. Soc. Japan*, 1945, **65**, 3; *Chem. Abs.*, 1951, **45**, 8528.
[14] Ishii, *J. Pharm. Soc. Japan*, 1952, **72**, 1315; *Chem. Abs.*, 1953, **47**, 12, 386.
[15] Ishii, *J. Pharm. Soc. Japan*, 1952, **72**, 665.
[16] Ochiai, Itai, and Yoshino, *Proc. Imp. Acad.* (*Tokyo*), 1944, **20**, 141; *Chem. Abs.*, 1954, **48**, 12,100.

*a*, Substituents are given. *b*, " S " indicates the standard conditions (cf. text). " T " indicates that 0·25 g. of the oxide in 15 c.c. of ethanol with 0·08 g. of Pd–C (5%) was used, but with conditions otherwise as above. " U " indicates that 0·41 g. of the oxide, 10 c.c. of ethanol, 4 c.c. of water, and 0·1 g. of catalyst were used. " V " indicates that the acid (0·5 g.) in 0·14N-aqueous sodium hydroxide (20 c.c.) was shaken over the catalyst (0·1 g.); after filtration and concentration addition of acetic acid gave the product. *c*, " P ", " L ", and " A " indicate that the reduction product was isolated respectively as picrate, picrolonate, or amide. " M " indicates that a mixed m. p. with an authentic specimen was not depressed. *d*, Brandes and Stoehr, *J. prakt. Chem.*, 1896, **54**, 488. *e*, Clemo and Gourlay, *J.*, 1938, 478. *f*, Hess and Grau, *Annalen*, 1925, **441**, 101. *g*, Haworth, Heilbron, and Hey, *J.*, 1940, 349. *h*, Found: C, 53·0; H, 3·1. Calc. for $C_{17}H_{12}O_7N_4$: C, 53·1; H, 3·1%. *j*, La Forge, *J. Amer. Chem. Soc.*, 1928, **50**, 2484. *k*, den Hertog and Overhoff, *Rec. Trav. chim.*, 1950, **69**, 468. *l*, With decomp. *m*, Wagstaff, *J.*, 1934, 276. *n*, Chiang and Hartnung, *J. Org. Chem.*, 1945, **10**, 21. *o*, Katritzky, *J.*, 1955, 2581. *p*, Katritzky and Monro, *J.*, in the press. *q*, Apparently a new polymorph. *r*, Clemo and Hogarth, *J.*, 1941, 41. *s*, Authentic ethyl *iso*nicotinate picrate separated from ethanol as a new *polymorph*, needles, m. p. 124—125° (Found: C, 44·2; H, 3·3; N, 15·0. $C_{14}H_{14}O_9N_4$ requires C, 44·2; H, 3·2; N, 14·7%). *t*, 4-Ethoxycarbonylpiperidine. *u*, Clemo and Metcalfe, *J.*, 1937, 1523. *v*, Found: C, 44·0; H, 4·8. Calc. for $C_{14}H_{18}O_9N_4$: C, 43·5; H, 4·7%. *w*, Badgett, Provost, Ogg, and Woodward, *J. Amer. Chem. Soc.*, 1945, **67**, 1135. *x*, Mixed m. p. with end-product of no. 36. *y*, den Hertog, Broekmann, and Combé, *Rec. Trav. chim.*, 1951, **70**, 105. *z*, 10% of starting material also recovered. *aa*, 3% of starting material also recovered. *ab*, *β-3-Pyridylpropionamide 1-oxide* formed rods from ethanol (Found: C, 57·9; H, 6·1. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·1%). *ac*, Graef, Fredericksen, and Burger, *J. Org. Chem.*, 1946, **11**, 257. *ad*, Authentic ethyl β-3-pyridylpropionate picrate separated from ethanol as a new *polymorph*, prisms (Found: C, 47·6; H, 3·8. $C_{16}H_{16}O_9N_4$ requires C, 47·1; H, 3·9%). *ae*, No. 20. *af*, No. 19. *ag*, Bergstrom, Norton, and Siebert, *J. Org. Chem.*, 1945, **10**, 452. *ah*, Authentic specimen prepared by treating ethyl β-3-pyridylpropionate with aqueous-methanolic ammonia, to give β-3-pyridylpropionamide as a new *polymorph*, plates (from ethanol), m. p. 117° (Found: C, 64·2; H, 6·7. $C_8H_{10}ON_2$ requires C, 64·0; H, 6·7%). *ai*, Livshits *et al.*, *J. Gen. Chem.* (*U.S.S.R.*), 1951, **21**, 1360; *Chem. Abs.*, 1952, **46**, 5051 (Found: C, 63·6; H, 6·2; N, 9·2. Calc. for $C_8H_9O_2N$: C, 63·6; H, 6·0; N, 9·3%). *aj*, *4-Phenethylpyridine 1-oxide*, prisms from ethyl acetate (Found: C, 78·7; H, 7·1. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·6%). *ak*, Found: C, 85·1; H, 7·1. Calc. for $C_{13}H_{13}N$: C, 85·2; H, 7·1%. *al*, Mixed m. p. with end-product of no. 29 not depressed. *am*, *2-Phenethylpyridine 1-oxide*, prisms from light petroleum (b. p. 40—60°) (Found: C, 78·7; H, 6·8. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·6%). *an*, Found: C, 55·5; H, 3·7. Calc. for $C_{19}H_{16}O_9N_4$: C, 55·3; H, 3·9%. *ao*, Katritzky, *J.*, 1956, 2404. *ap*, Treated with potassium carbonate in chloroform to remove hydrogen chloride. *aq*, Found: C, 41·3; H, 2·6; N, 16·9. Calc. for $C_{11}H_8O_8N_4$: C, 40·8; H, 2·5; N, 17·3%. *ar*, Fine suspension of substrate used. *as*, Pinner, *Ber.*, 1901, **34**, 4250. *at*, Frankenburg, Gottscho, Mayaud, and Tso, *J. Amer. Chem. Soc.*, 1952, **74**, 4309. *au*, Found: C, 44·6; H, 3·1. Calc. for $C_{13}H_{10}O_8N_4$: C, 44·6; H, 2·9%.

XUM

reduced more slowly than the corresponding 4-substituted compound, presumably because of steric hindrance. The ring was hydrogenated much more slowly (cf. no. 13).

(ii) The hydrogenation of compounds with a conjugated carbon–carbon double bond was next investigated. The 1-oxides of β-3- and -4-pyridylacrylic esters, amides, and acids and 4-styrylpyridine 1-oxide each absorbed two mols. of hydrogen at comparable rates, giving the corresponding saturated pyridine (nos. 17, 20, 23, 25—27, 29). Interruption after absorption of one mol. gave good yields of 4-phenethylpyridine 1-oxide (no. 28) and the pyridylpropionic amide 1-oxides (nos. 22, 24), and fair yields of the ester 1-oxides (nos. 16, 19); only mixtures were obtained from the acids. In 2-styrylpyridine 1-oxide (no. 31) the second molecule was absorbed only very slowly (incomplete after 3 days).

4-Chloropyridine 1-oxide absorbed 1 mol. of hydrogen, to give pyridine 1-oxide (nos. 33, 34), but both 3- and 4-acetylpyridine 1-oxide lost the oxide function before attack on the ketone group occurred (nos. 38, 39). It is of interest that 4-chloropyridine 1-oxide with iron–acetic acid gives 4-chloropyridine.[17] Previous work in this laboratory [5] has supported statements in the literature (above) that 4-nitro- and 4-benzyloxy-pyridine 1-oxide can be hydrogenated to 4-amino- and 4-hydroxypyridine 1-oxide. We now show that further reduction to the corresponding pyridines occurs readily (nos. 36 and 37).

(iii) 2- and 4-Styrylpyridine, β-3- and β-4-pyridylacrylic ester, and 4-chloropyridine were hydrogenated under the same conditions as their 1-oxides (nos. 18, 21, 30, 32, 35). The functional group was reduced at the same rate as, or a little slower than, in the 1-oxides.

The structures assigned to the reduction products are supported by infrared and ultraviolet spectra.

*Experimental.—Hydrogenations under standard conditions.* The substrate (0·01 mole) in ethanol (20 c.c.) over 5% palladium–charcoal (0·3 g.) was shaken under hydrogen at room temperature and pressure. After absorption of the required amount of hydrogen, or after absorption had ceased, catalyst was filtered off and washed with ethanol, and the filtrate and washings were evaporated, or the product, if volatile, was converted directly into a derivative.

This work was carried out during the tenure (by A. R. K.) of an I.C.I. Fellowship.

THE DYSON PERRINS LABORATORY,
OXFORD UNIVERSITY.

[*Received, September 26th*, 1957.]

[17] den Hertog and Combé, *Rec. Trav. Chim.*, 1951, **70**, 581.

---

## 249. *The Electric Dipole Moments of* 1 : 2-5 : 6-*Dibenzo*cyclo-*octadiene and* o-*Xylene.*

By E. W. RANDALL and L. E. SUTTON.

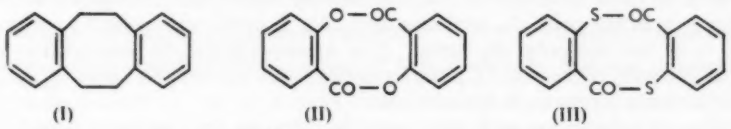
Electrical-polarisation measurements on benzene solutions of 1 : 2-5 : 6-dibenzo*cyclo*octadiene, at 25°, indicate that 25—35% of the solute is in the polar $C_{2v}$ conformation.

*X*-RAY analysis [1] shows that in the crystalline state 1 : 2-5 : 6-dibenzo*cyclo*octadiene (I) exists in the *trans*-conformation. On the other hand, measurements [2] of electric dipole moments show that the structurally somewhat similar disalicylide (II) in benzene solution exists in the *cis*-conformation, as do also di(thiosalicylide) [3] (III), the lactone of 2′-hydroxydibenzyl-2-carboxylic acid [4] (IV), and 1 : 6-dichloro*cyclo*octa-1 : 5-diene [5] (V). In order to

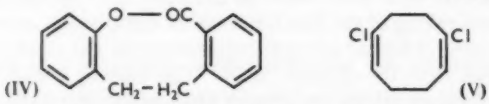
[1] Davidson, quoted by Baker, Banks, Lyon, and Mann, *J.*, 1945, 27.
[2] Edgerley and Sutton, *J.*, 1951, 1069.
[3] Saxby and Sutton, quoted by Baker, El Nawawy, and Ollis, *J.*, 1952, 3163.
[4] *Idem*, quoted by Baker, Ollis, and Zealley, *J.*, 1952, 1447.
[5] Roberts, *J. Amer. Chem. Soc.*, 1950, **72**, 3300.

elucidate the conformation of 1 : 2-5 : 6-dibenzo*cyclo*octadiene in solution, we have measured its electric dipole moment in benzene at 25°, and also that of *o*-xylene.

For *o*-xylene, ${}_TP - R_D$ is 8·0 ± 0·5 c.c. and, if ${}_AP$ is taken [6] as 1·9 c.c., μ can be calculated to be 0·54 D. This agrees well with the value we have recalculated from




(I) (II) (III)




(IV) (V)

Tiganik's measurements,[7] *viz.*, 0·53 D, using the modified Halverstadt–Kumler [8] procedure and the value for ${}_AP$ quoted above.

For 1.: 2-5 : 6-dibenz*cyclo*octadiene, ${}_TP - R_D$ is 9·4 ± 0·5 c.c., and ${}_AP$ is likely to be between 2 and 4 c.c., *i.e.*, about twice as great as for *o*-xylene, so that μ lies between 0·50 and 0·60 D. A comparative run with the non-polar substance *p*-xylene (${}_TP = 37{\cdot}28$ c.c., ${}_EP = 36{\cdot}20$ c.c.) showed that the above-determined value for ${}_OP$ is well outside the error due either to technique or to atom polarisation.

This indicates (i) that the substance in solution is not all in the non-polar, *trans*-conformation ($C_i$ point group) (Fig. 1 of ref. 1), (ii) that it is not all in the polar, *cis*-conformation ($C_{2v}$ point group) (Fig. 1*B* of ref. 1) which, when the moment of *o*-xylene is taken to be 0·54 D (see above) and it is assumed that the valency angles in the methylene groups are tetrahedral, would have a calculated moment of 1·01 D and an orientation polarisation of 20·84 c.c.

The polarisation data are consistent with the view that 25—35% of the substance is in the $C_{2v}$ form. The result is rather sensitive to the value chosen for the moment of *o*-xylene, for if the latter is taken as 0·62 D (the value for the gas [3]) the percentage range becomes 20—28%, and also to the value assumed for ${}_AP$, an increase of 1 c.c. therein leading to a decrease of about 4 in the percentage.

Baker, Banks, Lyon, and Mann [1] have illustrated another conformation (Fig. 1*A* of ref. 1) which can be made by twisting the $C_{2v}$ *cis*-form. This is of point group $D_2$ and should be both non-polar and enantiomorphic. There is thus the possibility of *four* conformational entities in solution, as well as, of course, intermediate forms. Baker, Banks, Lyon, and Mann [1] expressed the opinion, after examination of ordinary molecular models, that the rigid *trans*-conformation could be converted into the mobile *cis*-conformation only by passage through a highly strained intermediate or by breaking and re-forming a bond.

It does not seem possible to compare precisely the stabilities of these various conformations: there are two ethane residues in the molecule, and in all four conformations the bonds are eclipsed in each residue, so that one needs to know the relative interaction energies of two eclipsed C–H bonds, of two eclipsed C–Ph bonds, and of one C–H bond eclipsed by a C–Ph bond. The details of the numbers and kinds of eclipsed pairs for each conformation are in the annexed Table.

Eclipsed pairs of bonds.

| Conformation | CH and CH | CH and CPh | CPh and CPh |
|---|---|---|---|
| $C_i$ (*trans*) | 2 | 4 | 0 |
| $D_2$ | 2 | 4 | 0 |
| $C_{2v}$ (*cis*) | 4 | 0 | 2 |

[6] Hurdis and Smyth, *J. Amer. Chem. Soc.*, 1942, **64**, 2212.
[7] Tiganik, *Z. phys. Chem.*, 1931, *B*, **13**, 425.
[8] Everard, Hill, and Sutton, *Trans. Faraday Soc.*, 1950, **46**, 417.

XUM

Other repulsions, *e.g.*, van der Waals's, appear to be least for the *trans*-conformation. In the *cis*-model the benzene rings have overlapping $\pi$-electron clouds, and in the $D_2$ conformation two hydrogen atoms in each ethane residue interfere with two in the other ethane residue.

If there is no great difference in stability we may expect that, at equilibrium, 25% of the substance is in the polar $C_{2v}$ conformation, 25% is in the non-polar $C_i$ conformation, and 50% is in the non-polar $D_2$ forms. Our measurements and assumptions indicate between 25 and 35% of the polar $C_{2v}$ conformation; but all that can safely be said is that some polar *cis*-form is present in the solution.

No change of polarisation with time could be detected, the minimum period between making of the solution and taking of the first observation being of the order of 5 min. The energy of activation for establishment of equilibrium between the conformational entities therefore appears to be less than 15—20 kcal./mole. This may be because the interatomic repulsions in the stable conformations are greater than in intermediate ones, and partly compensate for the bond strains in the latter.

Roberts [5] has calculated that the energy barrier between the boat and the chair conformation of 1 : 6-dichloro*cyclo*octa-1 : 5-diene is 9 kcal./mole, while that between the boat and the skew conformation is 3—14 kcal./mole. Thus the conformations ought to be readily interconvertible at room temperature. His polarisation measurements indicate that at least 85% of the molecules are in the boat conformation despite a dipole–dipole repulsion in this form of approximately 500 cal./mole. He concludes that this predominance of the boat conformation is best accounted for by secondary valency forces. These may, of course, be considerably modified in the dibenzo-derivative, just as the formation of the transition state may be affected by a stiffening of the molecule by the benzene rings.

Another example which appears relevant is the formation of the *cyclo*octa-1 : 5-diene complexes $C_8H_{12}PtCl_2$ and $C_8H_{12}PdCl_2$ by reaction of the diolefin with $K_2PtCl_4$ and $Na_2PdCl_4$ respectively.[9] These are best formulated as chelate complexes in which the hydrocarbon has the boat conformation.[10] The reaction for the latter complex is rapid—" a yellow precipitate is formed almost at once "—so conversion of the *cyclo*octadiene in this case, if necessary, is evidently rapid.

## Experimental

The 1 : 2-5 : 6-dibenzo*cyclo*octadiene was kindly sent by Professor A. C. Cope, and had m. p. 108·5° (cf. ref.[1]). Its purity was checked further by analysis (Found: C, 92·1; H, 7·7. $C_{16}H_{16}$ requires C, 92·3; H, 7·7%) and by infrared spectroscopy which showed that no appreciable amount of methanol was present.

| 1 : 2-5 : 6-Dibenzo*cyclo*octadiene | | | | *o*-Xylene | | | |
|---|---|---|---|---|---|---|---|
| $10^4w$ | $\varepsilon$ | $v$ | $10^5\Delta n_D$ | $10^4w$ | $\varepsilon$ | $v$ | $10^5\Delta n_D$ |
| 2186 | 2·2736 | 1·1443 | 16 | 4049 | 2·2743 | 1·1446 | 0 |
| 3677 | 2·2745 | 1·1438 | 32 | 5697 | 2·2748 | 1·1446 | 2 |
| 5862 | 2·2755 | 1·1435 | 51 | 7508 | 2·2755 | 1·1447 | 1 |
| 7503 | 2·2763 | 1·1431 | 66 | 10165 | 2·2765 | 1·1446 | 1 |
| $\varepsilon = 2{\cdot}2726 + 0{\cdot}486w$; $v = 1{\cdot}1447 - 0{\cdot}213w$; $\Delta n_D = -0{\cdot}00001 + 0{\cdot}089w$; $_EP = 67{\cdot}58$ c.c.; $_TP = 76{\cdot}94$ c.c. | | | | $\varepsilon = 2{\cdot}2727 + 0{\cdot}371w$; $v$ and $\Delta n_D$ show very small variation with $w$. $_EP = 35{\cdot}66$ c.c.; $_TP = 43{\cdot}62$ c.c. | | | |

*o*-Xylene (from Messrs. L. Light and Co.) was used without further purification. Not only is the moment of *o*-xylene small and the experimental error in $\mu$ consequently large, but the principal impurities (*m*- and *p*-xylene, and ethylbenzene) all have small moments, so that relatively large amounts of these impurities would not vitiate the determination; *e.g.*, 3% of

[9] Chatt, Vallarino, and Venanzi, *J.*, 1957, 2496.
[10] Jensen, *Acta Chem. Scand.*, 1953, **7**, 866, 868.

*p*-xylene impurity would lead to an error of only 0·01 D. The sample had $n_D^{25}$ 1·5031 (lit.,[11] 1·5029) and $d_{25}$ 0·8759 (lit.,[11] 0·87596).

Other details of the measurements and the nomenclature have been described.[12]

We thank Professor Wilson Baker, F.R.S., and Dr. W. D. Ollis for helpful discussions, and Mr. D. R. Eaton for the infrared measurements.

THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, October 4th*, 1957.]

[11] Weissberger, Proskauer, Riddick, and Toops, "Organic Solvents," 2nd edn., Interscience Publ. Inc., New York, 1955.
[12] Katritzky, Randall, and Sutton, *J.*, 1957, 1769.

---

## 250. *Differential Capacity Measurements in Aqueous and Methanolic Ammonium Chloride, Ammonium Fluoride, and Hydrochloric Acid in Relation to Anion Adsorption.*

By A. A. MOUSSA, H. M. SAMMOUR, and H. A. GHALY.

Differential capacities were measured in 0·1N-$NH_4Cl$ and -$NH_4F$ and in 1·0-, 0·3-, and 0·1-N-HCl, in water and methanol. For the first two electrolytes, in both solvents, earlier results were confirmed, and the method usually followed in interpreting the minimum capacity observed with increasing cathodic polarisation is discussed. In aqueous and methanolic hydrochloric acid solutions, reduction of hydrogen ions prevented extension of the measurements, and no capacity minima were observed within the cathodic potential range corresponding to ideal polarisation. The electrocapillary curves of mercury in the latter solutions were obtained. From the rate of change of the interfacial tension with the chemical potential of HCl, surface excesses of chloride ions were calculated for aqueous and methanolic 0·3N-hydrochloric acid, and the results compared.

GRAHAME [1] reported measurements of the differential capacity of the electrical double layer between mercury and methanolic salt solutions of ammonium chloride, fluoride, and nitrate. The outstanding features of the curves obtained for 0·1N-solutions are, first, the complete disappearance of the hump characteristic of the curves obtained in the corresponding aqueous solutions; secondly, the relatively low minimum capacity value, $C_{min.}$, of 9·0 μF/cm.$^2$ observed on the cathodic potential side compared with that observed in aqueous solutions, *viz.*,[2] 15·5—16·0 μF/cm.$^2$. At potentials less cathodic than that corresponding to $C_{min.}$, the curves diverged because of the specific adsorption of anions ($Cl^-$), but they coincided almost exactly at more cathodic potentials. Because of this similarity in behaviour, and by comparison with that observed in aqueous solutions, $C_{min.}$ was considered to indicate complete repulsion of any specifically adsorbed charge from the metal surface. Grahame pointed out that conclusive evidence could be obtained from the rate of change of the differential capacity with chemical potential, but the necessary data, the activity coefficient values in methanol, are lacking. From surface-tension measurements in aqueous and methanolic hydrochloric acid solutions, Parsons and Devanathan [3] had shown that anions are less readily repelled from a negatively charged mercury surface in methanol than in water. In methanol positive adsorption of the $Cl^-$ ions even at potentials corresponding to hydrogen evolution was reported, a result apparently not in accordance with Grahame's conclusion.

We measured differential capacities in 0·1N-aqueous and -methanolic ammonium chloride and fluoride under conditions differing only in minor details from those used by

[1] Grahame, *Z. Elektrochem.*, 1955, **59**, 740.
[2] Grahame, Poth, and Cummings, *J. Amer. Chem. Soc.*, 1952, **74**, 4422.
[3] Parsons and Devanathan, *Trans. Faraday Soc.*, 1953, **49**, 673.



XUM

Grahame. Measurements were also made in aqueous and methanolic 1·0, 0·3, and 0·1N-hydrochloric acid with a view to ascertain whether any evidence for the complete repulsion of anions from the interface could be obtained; the experimental conditions were such as to enable also the calculation of anion surface excesses.

## Experimental

Grahame's a.c. bridge technique of measuring the differential capacity of a spreading mercury surface [4] was used, but we adopted a simpler method of measuring area at the end of the drop time. The method has been repeatedly checked by Professor Grahame who did not find any difference between the results obtained at the end of the drop time and those obtained few tenths of a second earlier.[5] According to our procedure, in one solution and at constant polarisation, when the resistance $R$ and the capacity $C$ on the known arm of the bridge are adjusted at appropriate values, there is observed on the screen of the oscilloscope only one state of balance during the whole life of the mercury drop; $C$ and $R$ will then determine the apparent impedance corresponding to the area at that particular stage of growth at which balance occurs. By setting $R$ at a higher or a lower value and adjusting $C$, the state of balance could be made to correspond to an earlier or a later stage of growth respectively. With $R$ at its lowest possible value, $C$ is assumed to correspond to the area at the end of the drop time.

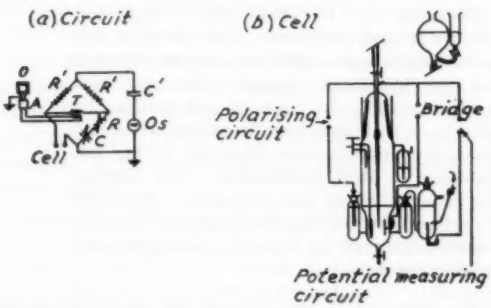



Fig. 1.

*O, Cossor-type oscilloscope.*
*A, Two-stage audio-amplifier.*
*R', 1000 Ohm non-inductive resistances.*
*R, 11,111 Ohm standard resistance box.*
*C, Decadic condenser, 0·0001—3·0 μF.*
*Os, R.C. Oscillator.*
*C', 0·1μF Condenser.*
*T, Audio-transformer.*

The various components of the bridge used, and the cell in which measurements were performed were as shown in Fig. 1(*a*) and (*b*), respectively. The input to the bridge was 5 mV, and measurements were all made at 1000 cycles/sec. In aqueous hydrochloric acid the potential of the dropping-mercury cathode was varied with respect to a mercury anode in the same solution, an ordinary potentiometer being used in series with a mirror Onwood micro-ammeter. The potentiometer readings served only to indicate extent of polarisation. In the methanolic acid solutions the potential of the cathode was varied with respect to an auxilliary graphite electrode. In both solutions the potential of the mercury cathode against a hydrogen electrode in the same solution was registered on a valve circuit. In aqueous and methanolic ammonium chloride the mercury cathode was polarised directly against a decinormal calomel electrode in water. A filter-paper plug was used to minimise mixing of solvents. In ammonium fluoride solutions it was essential, with the type of cell used, to replace the calomel electrode by a mercury–mercurous sulphate electrode in aqueous 0·2M-sodium sulphate so as to eliminate the effect of $Cl^-$ ions.

The rate of flow of mercury was determined in each solution under exactly the same conditions as were subsequently followed during the measurements, from the mass and drop time of one hundred drops collected at open circuit. At each polarisation the time necessary for five drops to form was measured accurately to 0·1 sec. and an area factor was computed.

*Materials.*—Mercury ("Carlo Erba") was purified by standard methods, then thrice distilled under vacuum. Methanol (Merck's "pro analysi") was distilled once before use. A stock solution of hydrogen chloride in methanol was diluted as required. The aqueous acid solutions were prepared from a twice-distilled constant-boiling mixture. Ammonium chloride and fluoride ("AnalaR") were used as supplied.

[4] Grahame, *J. Amer. Chem. Soc.*, 1941, **63**, 1207.
[5] *Idem*, personal communication.

The cell and its accessories, including the mercury reservoir, were all accommodated in an air thermostat provided with a sliding-front glass door. Measurements were all made at 25° ± 0·5°.

## Results and Discussion

For the aqueous and methanolic ammonium salt solutions our results agree excellently with Grahame's.[1,2] Well-defined minimum capacities amounting, respectively, to 16·1 and 15·6 μF/cm.² in water and to 9·0 μF/cm.² for both electrolytes in methanol, were obtained. The corresponding potentials, with respect to the unpolarisable reference electrodes used, were −1·20 and −1·45 v in the aqueous solutions, and −0·90 and −1·15 v in the methanolic ones. For electrolytes which exhibit specific anion adsorption, $C_{min.}$ is usually considered to indicate complete repulsion of any specifically adsorbed charge, and according to Grahame,[6] the relation

$$1/C_{min.} = 1/C^0 + 1/C^d \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

holds, $C^0$ being the differential capacity of the charge-free space between the mercury surface and the electrolyte, and $C^d$ that of the diffuse part of the electrical double layer. In 0·1N-solutions of uni-univalent electrolytes at 25°, the latter is given (in μF/cm.²) by

$$C^d = 19{\cdot}47(q_M^2 + 0{\cdot}174D)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $q_M$ is the total surface charge density in μcoul./cm.², and $D$ is the dimensionless dielectric constant of the solvent. From our results in aqueous solutions, although equations (1) and (2) yielded a $C^0$ value of 17·1 μF/cm.² in agreement with values previously reported,[7] yet this was not so, *e.g.*, in methanolic solutions. For $C^0$ in methanol Grahame reported 9·2 μF/cm.², but when this is combined with the value for $C_{min.}$ of 9·0 μF/cm.², eqn. (1) gives $C^d = 414$ μF/cm.², a physically unacceptable value since from eqn. (2), $D$ for methanol being taken as 32·5, $q_M$ would be about 20 μcoul./cm.². The value experimentally obtained, however, was 5·7 ± 0·5 μcoul./cm.². Two consequences follow. By substituting the experimental $q_M$ value in eqn. (2), and combining the result with the observed value of $C_{min.}$, which is the procedure usually followed, $C^0$ will be found to be 9·8 μF/cm.², a value which is higher than that reported by Grahame. Alternatively, if $C^d$ as obtained from eqn. (2), by using the presumably accurate $q_M$ value of 5·7 μcoul./cm.², is combined with Grahame's value of 9·2 μF/cm.² for $C^0$, $C_{min.}$ would then be ≃ 8·7 μF/cm.² as compared with the experimentally observed value of 9·0 μF/cm.²: the difference is believed to be outside the limits of experimental error even with our relatively simple technique. However, it is possible that Grahame's theory does not apply strictly in solvents other than water.

The results of the differential capacity measurements in the aqueous and methanolic hydrochloric acid are shown in Fig. 2. On the cathodic side, measurements were extended only to those potential values indicated. Over the potential range used, the mercury–solution interface was believed to be ideally polarised. At more cathodic potentials a sudden rise in the charging d.c. current occurred, and the resistance values which gave balance showed simultaneously a marked increase. With the sort of a.c. bridge used, the above observations simply indicate leakage through the electrical double layer condenser as a result of a continuous discharge of $H_3O^+$ ions.[8] It was therefore considered unjustifiable to extend the measurements to more negative potentials under conditions which would limit the applicability of equations (1) and (2). Parsons and Devanathan [3] extended their surface-tension measurements to potentials as negative as −0·950 v. This, however, was intended by the authors for comparing the results of measurements of the rate of an electrode reaction with those derived from measurements at an approximately ideal polarised electrode. As judged from the present measurements, the differential

[6] Grahame, *Chem. Rev.*, 1947, **41**, 441.
[7] Devanathan, *Trans. Faraday Soc.*, 1954, **50**, 373.
[8] Frumkin, *Acta Physicochim. U.R.S.S.*, 1940, **13**, 799.



XUM

capacity curves for the various acid concentrations used tend to converge on the negative potential side, in both water and methanol, to a low common capacity value, but no well-defined minima which would indicate complete repulsion of the specifically adsorbed charge are observed over the potential range corresponding to ideal polarisation. Since in

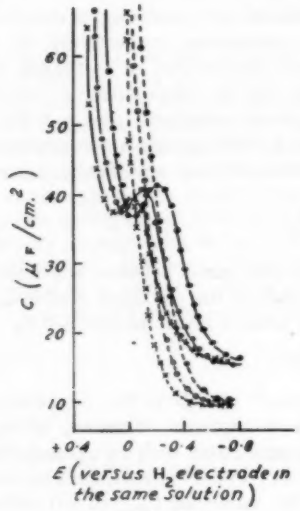



FIG. 2. *Differential capacity in the solutions: full lines, aqueous; broken lines, methanolic solution.*
×, 0·1N-HCl; ○, 0·3N-HCl; ●, 1·0N-HCl.

FIG. 3a.

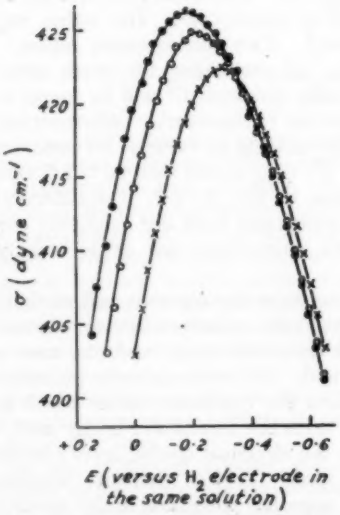



FIG. 3b.

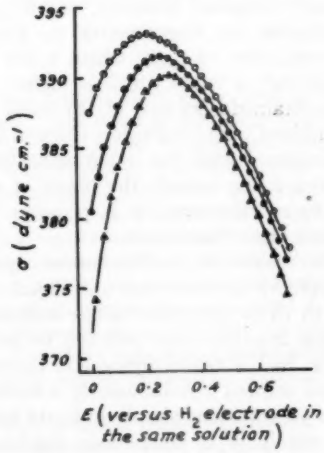



FIG. 3. *Electrocapillary curves in* (a) *aqueous solutions*: ●, 0·1N-HCl; ○ 0·3N-HCl; ×, 1·0N-HCl; *and* (b) *methanolic solutions*: ○, 0·1N-HCl; ●, 0·3N-HCl; ▲, 1·0N-HCl.

these solutions, measurements were made with respect to an electrode which is reversible to cations in the same solution, and the data for the activity coefficients in both solvents are available, the surface excess of the $Cl^-$ ions, $\Gamma$, may be readily obtained [9] from

$$-(d\sigma/du)_\pi = \Gamma \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

[9] Ref. 6, p. 458.

where $u$ is the chemical potential of HCl, $\sigma$ is the interfacial tension, and $E$ is the measured potential. The $\sigma$ values as a function of $E$ were derived on the basis of the well-known thermodynamic relations:

$$-\mathrm{d}^2\sigma/\mathrm{d}E^2 = \mathrm{d}q_M/\mathrm{d}E = C \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

or

$$\iint_{E\,\mathrm{e.c.m.}}^{E} C \,.\, \mathrm{d}^2E = \int_{E\,\mathrm{e.c.m.}}^{E} q_M \,.\, \mathrm{d}E = \Delta\sigma \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The values chosen for the co-ordinates of the electrocapillary maxima were those of Parsons and Devanathan. The electrocapillary curves obtained for the aqueous and methanolic solutions are presented graphically in Figs. 3(*a*) and (*b*). Direct comparison with previous results is not possible since in this case the $\Delta\sigma$ values are in fact the quantities that need to be compared. However, for the methanolic solutions, for example, the absolute $\sigma$ values over almost the whole potential range used scarcely differ from those obtained by Parsons and Devanathan by more than 0·5 dyne, which is the limit of accuracy

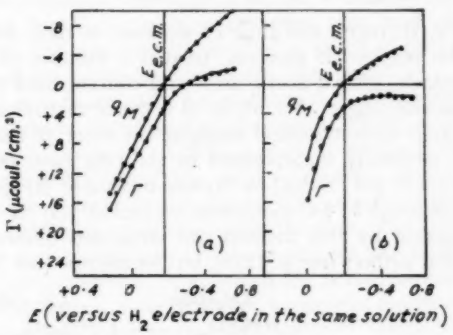



FIG. 4. *Surface excess, Γ, in* 0·3N-HCl: (*a*) *aqueous,* (*b*) *methanolic.*

with which the values can be read from their curves. The agreement is considered highly satisfactory for two sets of results obtained from two basically different methods of measurement.

From the rate of change of the interfacial tension with the chemical potential as given by equation (3), Γ values at 50 mv intervals were obtained for aqueous and methanolic 0·3N-hydrochloric acid. The activity coefficient values for the aqueous solutions were computed from Harned and Ehlers's data at 25°.[10] For 1·0, 0·3, and 0·1N-hydrochloric acid the values used were 0·809, 0·755, and 0·796 respectively. Those for the methanolic solutions were computed from Nonhebel and Hartley's data,[11] the corresponding values being 0·319, 0·343, and 0·437 respectively. In Fig. 4(*a*) and (*b*), the Γ values obtained are shown plotted against the polarising potential $E$. On the same figure the corresponding $q_M$ values are also shown. As can be seen from these results, Parsons and Devanathan's conclusion that chloride ions are less readily repelled from a negatively charged mercury surface in the methanolic than in the aqueous solution is further confirmed. If the positive adsorption observed in the methanolic solutions is to be ascribed to undissociated hydrogen chloride molecules rather than chloride ions, as suggested by Grahame,[12] this probably would have had its effect also at the uncharged mercury surface, which can hardly be deduced from the results of the present measurements.

FACULTY OF SCIENCE,
UNIVERSITY OF CAIRO.

[*Received, July 8th,* 1957.]

[10] Harned and Ehlers, *J. Amer. Chem. Soc.*, 1933, **55**, 2179.
[11] Conway, "Electrochemical Data," Elsevier Publishing Co., London, 1952, p. 94.
[12] Grahame, *Ann. Rev. Phys. Chem.*, 1955, **6**, 352.

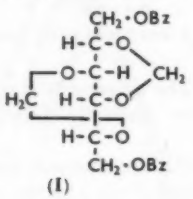
XUM

## 251. *Studies of Trifluoroacetic Acid. Part XIV.* Reaction of Acyl Trifluoroacetates with* 1 : 6-*Di*-O-*benzoyl*-2 : 4-3 : 5-*di*-O-*methylene*-D-*glucitol.*†

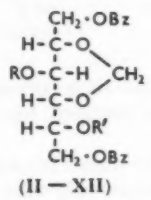
By E. J. Bourne, J. Burdon, and J. C. Tatlow.

An equimolecular mixture of acetic (or benzoic) acid and trifluoroacetic anhydride reacts at 25° with 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol to give 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (or 1 : 5 : 6-tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol). Prolonged reaction at 25° does not cause scission of the βC-ring (see Barker and Bourne [1] for this nomenclature). A ten-fold excess of acetic acid over trifluoroacetic anhydride gives 3-*O*-acetoxymethyl-5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol. Conformational analysis is used to explain the position of ring scission and the marked difference in reactivity between the rings.

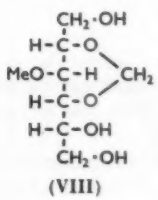
Hann, Hudson, and their co-workers, in their studies on the structures of cyclic acetals of the polyhydric alcohols, treated a number of such acetals with a mixture of acetic anhydride, glacial acetic acid, and concentrated sulphuric acid, which caused rupture of the acetal rings. Acetolysis of a cyclic methylene ether left an *O*-acetyl group on one, and an *O*-acetoxymethyl group on the other, of the oxygen atoms of the polyalcohol which were originally incorporated in the ring (see, *inter alia*, refs. 1—5). Thus, 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol (I) gave 3-*O*-acetoxymethyl-5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (II) in 72% yield.[4] [When we prepared this compound by this method, its properties differed somewhat from those given by the original authors (see p. 1278), but we assume that both products had structure (II).]



(I)



(II — XII) except (VIII)



(VIII)

| | R | R′ |
|---|---|---|
| II | $CH_2{\cdot}OAc$ | Ac |
| III | Ac | Ac |
| IV | H | H |
| V | H | Ac |

| | R | R′ |
|---|---|---|
| VI | Ac | H |
| VII | Me | Ac |
| IX | Bz | Ac |

| | R | R′ |
|---|---|---|
| X | H | Bz |
| XI | Ac | Bz |
| XII | $CH_2{\cdot}O{\cdot}CO{\cdot}CF_3$ | Ac |

It appeared that an equimolecular mixture of trifluoroacetic anhydride and a carboxylic acid might react analogously with a cyclic methylene ether, with the introduction of acyl and trifluoroacetoxymethyl groups, since ions of the type $R{\cdot}CO^+$, which are required for acetolysis, are formed in such a mixture:

$$R{\cdot}CO_2H + (CF_3{\cdot}CO)_2O \rightleftharpoons R{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3 + CF_3{\cdot}CO_2H \quad . \quad . \quad . \quad . \quad (1)$$

$$R{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3 \rightleftharpoons R{\cdot}CO^+ + CF_3{\cdot}CO_2^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

* Part XIII, *J.*, 1957, 315.
† Presented in part at XIVth International Congress of Pure and Applied Chemistry, Zürich, 1955.

[1] Barker and Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 137.
[2] Hann and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 1906.
[3] Ness, Hann, and Hudson, *ibid.*, pp. 665, 670.
[4] Hann, Wolfe, and Hudson, *ibid.*, p. 1898.
[5] Haskins, Hann, and Hudson, *ibid.*, 1945, **67**, 1800; 1947, **69**, 624.

These equilibria have been suggested previously [6,7] to explain other reactions of mixtures of carboxylic acids and trifluoroacetic anhydride and have been confirmed by conductimetric,[8] infrared,[9] and cryoscopic [9] measurements.

When 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol (I) was treated with a nine-fold excess (necessary for complete dissolution) of an equimolecular mixture of acetic acid and trifluoroacetic anhydride for 3 hr. at 25° (the rotation had then become constant), a fluorine-containing syrup was formed. This compound decomposed on exposure to air with the evolution of formaldehyde and trifluoroacetic acid, but on being treated with dry methanol, as described by Bourne, Tatlow, and Tatlow [10] for the removal of *O*-trifluoroacetyl groups, it gave quantitatively a crystalline substance (A), m. p. 149—150°, which analysis indicated was an *O*-acetyldi-*O*-benzoyl-*O*-methylenehexitol. Its catalytic de-esterification with sodium methoxide in methanol gave the known 2 : 4-*O*-methylene-D-glucitol. Acetylation with acetic anhydride in pyridine gave a compound which was shown to be 3 : 5-di-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (III) as follows: 2 : 4-*O*-Methylene-D-glucitol was preferentially benzoylated at the primary hydroxyl groups with 2 mol. of benzoyl chloride in pyridine (a similar technique had been used by Hudson's group [11] to convert 2 : 5-*O*-methylene-D-mannitol into its 1 : 6-di-*O*-benzoyl derivative [12]). The dibenzoate (IV) was acetylated to give the 3 : 5-di-*O*-acetyl derivative (III), which was identical with the compound previously obtained.

Thus, compound (A) was 5-*O*- (V) or 3-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (VI). That it was the former was demonstrated in three ways. First, controlled acidic hydrolysis of 3-*O*-acetoxymethyl-5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol [3,4] (II) gave a product identical with (A) in 28% yield. Secondly, methylation of (A) with the Purdie reagents gave an *O*-methyl derivative (VII), which afforded an *O*-methyl-2 : 4-*O*-methylene-D-glucitol (VIII) by catalytic de-esterification: this could not have been the 5-*O*-methyl derivative as it consumed 1 mol. of sodium periodate with evolution of approximately 1 mol. of formaldehyde. Compound (A) is not proved to be the 5-acetate (V) by this etherification procedure alone, however, because of the possibility of acetyl migration from position 3 to position 5 during the methylation.[13] Final confirmation of structure (V) was provided however, as will be described in detail in a subsequent paper, by synthesis from 5-*O*-acetyl-6-*O*-benzoyl-1 : 3-2 : 4-di-*O*-methylene-D-glucitol and benzoic acid–trifluoroacetic anhydride.

Compound (V) could not be benzoylated very successfully with benzoyl chloride in pyridine at room temperature, but on being treated with benzoic acid–trifluoroacetic anhydride for 2 hr. at 60°, it afforded the 3-*O*-benzoyl derivative (IX) in good yield, the 2 : 4-methylene bridge (βC) remaining intact. This relative resistance to benzoylation is interesting. It is true that the 3-hydroxyl group is axial with respect to the acetal ring and that axial hydroxyl groups in *cyclo*hexane derivatives are difficult to esterify;[14] but this difficulty is usually attributed to steric hindrance by a pair of β-hydrogen atoms and this effect cannot be operative in a cyclic acetal since the β-positions are occupied by the ring oxygens.[15] Nevertheless, several compounds similar to (V), such as 2 : 4-*O*-benzylidene-xylitol [16] and 2 : 4-*O*-methylene-D-glucitol,[17] resist complete benzoylation, whereas the 2 : 4-*O*-methylene derivatives of ribitol [2] and D-talitol,[5] in which the 3-hydroxyl groups are

[6] Bourne, Randles, Tatlow, and Tedder, *Nature*, 1951, **168**, 942.
[7] Bourne, Randles, Stacey, Tatlow, and Tedder, *J. Amer. Chem. Soc.*, 1954, **76**, 3206.
[8] Randles, Tatlow, and Tedder, *J.*, 1954, 436.
[9] Bourne, Stacey, Tatlow, and Worrall, *ibid.*, p. 2006; Bourne, Tatlow, and Worrall, *J.*, 1957, 315.
[10] Bourne, Tatlow, and Tatlow, *J.*, 1950, 1367.
[11] Ness, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1943, **65**, 2215.
[12] Cf. also Müller, *Ber.*, 1932, **65**, 1055.
[13] Cf. Haworth, Hirst, and Teece, *J.*, 1930, 1405; 1931, 2858.
[14] Eliel, *Experientia*, 1953, **9**, 91.
[15] Cf. Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 2.
[16] Hann, Ness, and Hudson, *J. Amer. Chem. Soc.*, 1946, **68**, 1769.
[17] Bourne and Wiggins, *J.*, 1944, 517.

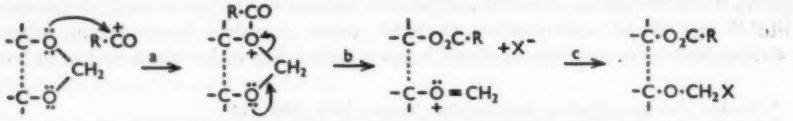
XUM

equatorial, apparently do not. However, 2 : 4-*O*-methylenexylitol, in which the 3-hydroxyl group is axial, as in (V), can be fully benzoylated easily in high yield.[3] Clearly the ease of benzoylation of the 3-hydroxyl groups in these compounds is not determined solely by their axial or equatorial arrangements and other substituents on the acetal rings must play a part. Models reveal that if three large groups are present in positions 1, 5, and 6 of 2 : 4-*O*-methylene-D-glucitol access of reagents to position 3 is hindered. During benzoylation of 2 : 4-*O*-benzylidenexylitol, the benzylidene and 1 : 5-di-*O*-benzoyl groups together act in a similar way, but in the methylene analogue the two ester groups alone do not provide an adequate shield. Models also show that approach to the equatorial 3-position during benzoylation of the 2 : 4-*O*-methylene derivatives of ribitol and D-talitol is not blocked by ester groups introduced preferentially at the other positions. That compound (V) can be acetylated easily in pyridine at room temperature is probably due to the difference in size of the acetyl and benzoyl groups.

Reaction of 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol with a nine-fold excess of an equimolecular mixture of benzoic acid and trifluoroacetic anhydride for 12 hr. at 25° (these conditions were chosen arbitrarily) afforded, after treatment with water, a 64% yield of a tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol identical with that prepared by Bourne and Wiggins [17] by Schotten–Baumann benzoylation of 2 : 4-*O*-methylene-D-glucitol. It seemed reasonable to assume that benzoic acid had reacted in the same way as acetic acid during fission of the βT-acetal ring and also that it was the 3-hydroxyl group which was resistant in the direct benzoylation of 2 : 4-*O*-methylene-D-glucitol; on both arguments the product was 1 : 5 : 6-tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (X). This was confirmed by acetylation when the product obtained was different from the 5-*O*-acetyl-1 : 3 : 6-tri-*O*-benzoyl derivative (IX) described above and must have been therefore 3-*O*-acetyl-1 : 5 : 6-tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (XI). The alkaline conditions used by Bourne and Wiggins [17] in the preparation of their compound (X) suggest that migration of benzoyl groups was extremely unlikely during its subsequent acetylation.

Prolonged treatment of the di-*O*-methylene compound (I) with acetic acid and trifluoracetic anhydride (24 hr. at 25°) did not result in much scission of the βC-ring since the mono-*O*-methylene product (V) was obtained as before, in only slightly diminished yield (92%). This conforms with earlier observations that βC-rings are, in general, far more stable than βT-rings. Nevertheless, it is remarkable that only the βT-ring of the acetal (I) should break and, further, that it should do so entirely in the one direction, and we advance the following explanation.

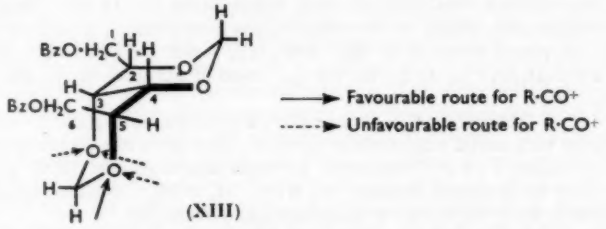
The βT-ring will presumably first form an oxonium complex with the $R{\cdot}CO^+$ ions which occur in acetolysis [cf. (a)]. Scission can then occur (b) in a manner similar to that suggested by Ingold [18] for the hydrolysis of simple acetals. The positive charge on the intermediate will be distributed between an oxonium and a carbonium cation, and will be neutralized (c) by the addition of $X^-$ to give the final product. For example, with acetic



anhydride, acetic acid, and concentrated sulphuric acid, $R{\cdot}CO^+$ will be $Ac^+$, and $X^-$ will be $AcO^-$. With an equimolecular mixture of a carboxylic acid and trifluoroacetic anhydride, the ions will be $R{\cdot}CO^+$ and $CF_3{\cdot}CO_2^-$. The unstable syrup formed initially in the reaction of the acetal (I) with acetic acid and trifluoroacetic anhydride was very probably 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-3-*O*-trifluoroacetoxymethyl-D-glucitol (XII), the trifluoroacetoxymethyl group of which would be extremely unstable.

[18] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, Ltd., London, 1953, p. 334.

The most favoured conformation (XIII) of the acetal (I) is analogous to that of *cis*-decalin and with the oxygens " inwards " (other conformations involve greater steric interactions). It is clear from Mills's arguments [15] that the 2 : 4-*O*-methylene ring (βC) should be relatively stable as it has the large $CH_2$·OBz group in an equatorial position, and that the 3 : 5-ring (βT) should be relatively unstable as the $-CH_2$·OBz group is axial here. The reason for the attack of R·$CO^+$ on the βT-ring at position 5, and not at 3, becomes apparent also, in the following manner: Oxonium ions are pyramidal [19] with bond angles of about 110° and so theoretically the R·$CO^+$ ion can bond with oxygen atoms at positions 3 and 5 in the normal equatorial or axial directions (see XIII). The two axial directions can be ruled out for the usual conformational reasons and the equatorial direction on the oxygen at 3 also, as there would be a considerable non-bonded interaction between the R·CO group and the $CH_2$·OBz group joined to position 2, in a similar manner to the well-known axial–axial 1 : 3-interaction of *cyclo*hexane conformational analysis. The only unhindered position left is the equatorial direction at the 5-oxygen, which would lead, after removal of the trifluoroacetoxymethyl group, to the formation of compound (V) or (X), only. This is also borne out by the use of atomic models, when it is possible to form an oxonium complex at oxygen 5 but not at oxygen 3. The possibility that a significant amount of ring scission had occurred by utilisation of the 3-oxygen atom, to give the 3-*O*-acetyl-5-*O*-trifluoroacetoxymethyl derivative, which by methanolysis afforded initially the 3-acetate and then, by migration, the 5-acetate (V), is therefore remote; moreover acyl groups which are prone to migrate have not been observed to do so during methanolysis.[20, 21]




(XIII)

Another effect occurred when a 10 : 1 molar ratio of acetic acid to trifluoroacetic anhydride was used in reaction with the diacetal (I) for 12 hr. at 25°: this gave 3-*O*-acetoxymethyl-5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol [4] (II) in 90% yield. The following explanation is advanced. Here an equilibrium (3), additional to (1) and (2), becomes important. In (1) the equilibrium position is almost 100% to the right and in (3) about 80%, in the presence of excess of acetic acid.[9] The 10 : 1 mixture therefore consists essentially of a mixture of acetic acid and acetic anhydride in the presence of a strong acid, trifluoroacetic. This is the same as the Hudson acetolysis mixture save that the concentrated sulphuric acid is replaced by trifluoroacetic, and it reacts in the same way. It affords a useful experimental confirmation of the correctness of equation (3).

$$AcOH + CF_3{\cdot}CO{\cdot}OAc \rightleftharpoons Ac_2O + CF_3{\cdot}CO_2H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

It seems from the above results that mixtures of carboxylic acids and trifluoroacetic anhydride are likely to have wide application for the cleavage of cyclic acetals under mild conditions and often with a high degree of specificity. An important advantage over the usual methods of acetolysis is that trifluoroacetoxy-groups in the products can be removed with methanol alone, without detriment to other groups, whereas the removal of acetoxy-groups requires more drastic conditions, resulting in low overall yields.

[19] Walsh, *J.*, 1953, 2296; Ferriso and Hornig, *J. Chem. Phys.*, 1955, **23**, 1464.
[20] Bourne, Huggard, and Tatlow, *J.*, 1953, 735.
[21] Bourne, Stacey, Tatlow, and Tatlow, *J.*, 1951, 826.

XUM

## Experimental

1 : 6-*Di*-O-*benzoyl*-2 : 4-3 : 5-*di*-O-*methylene*-D-*glucitol*.—Prepared by the method of Hann, Wolfe, and Hudson,[4] this compound had m. p. 159—160° and $[\alpha]_D^{14}$ +17·7° (*c* 2·31 in $CHCl_3$). These authors gave m. p. 158—159° and $[\alpha]_D$ +18·7° (in $CHCl_3$).

5-O-*Acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—(*a*) A solution of 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol (0·50 g.) in trifluoroacetic anhydride (1·50 ml., 9 mol.) and glacial acetic acid (0·62 ml., 9 mol.) was kept at 25° for 3 hr. (constant rotation). Volatile material was then removed *in vacuo* and the residual syrup was co-distilled once with dry carbon tetrachloride. The product, presumably 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-3-*O*-trifluoroacetoxymethyl-D-glucitol, was a syrup, which decomposed very rapidly with evolution of formaldehyde. No attempt was made to purify this compound and it was refluxed *in situ* with dry methanol (15 ml.) for 1 hr. Evaporation of the methanol left a white wax which gave, on crystallization from ethanol, 5-O-*acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol* (0·54 g.), m. p. 149—150°, $[\alpha]_D^{17}$ +4·2° (*c* 4·35 in $CHCl_3$) (Found: C, 62·1; H, 5·7%; N-alkali uptake, 6·89 ml./g. $C_{23}H_{24}O_9$ requires C, 62·2; H, 5·4%; N-alkali uptake, 6·76 ml./g.). Even after 24 hr. at 25° a 92% yield of this same product was obtained.

(*b*) The reaction mixture was prepared as in (*a*) but, after being kept at 25° for 3 hr., it was poured into sodium hydrogen carbonate solution. The solution was extracted with chloroform, and the extracts were washed with water, dried ($MgSO_4$), and evaporated. The residue, recrystallized from ethanol, gave 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·50 g.), m. p. 149—150°, alone and on admixture with the product obtained in (*a*).

2 : 4-O-*Methylene*-D-*glucitol*.—5-*O*-Acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·20 g.) was dissolved in dry methanol (10 ml.) in which a small piece of sodium had been dissolved, and the solution was kept at room temperature for 14 hr. Evaporation of the methanol left a white solid, which, on recrystallization from ethanol, gave 2 : 4-*O*-methylene-D-glucitol (0·08 g.), m. p. and mixed m. p. 163—164°, $[\alpha]_D^{21}$ −9·9° (*c* 1·00 in $H_2O$) (Found: C, 43·4; H, 7·3. Calc. for $C_7H_{14}O_6$: C, 43·3; H, 7·3%). Ness *et al.*[3] gave m. p. 163—164° and $[\alpha]_D$ −9·8° (in $H_2O$).

*Acetylation of* 5-O-*Acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—This compound (0·40 g.), acetylated with acetic anhydride in pyridine, gave, after recrystallization from aqueous ethanol, 3 : 5-*di*-O-*acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol* (0·37 g.), m. p. 185°, $[\alpha]_D^{17}$ +9·6° (*c* 1·42 in acetone) (Found: C, 61·8; H, 5·5%; N-alkali uptake, 8·12 ml./g. $C_{28}H_{26}O_{10}$ requires C, 61·7; H, 5·4%; N-alkali uptake, 8·23 ml./g.).

1 : 6-*Di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—Benzoyl chloride (0·89 ml., 2 mol.) was added dropwise to an ice-cold solution of 2 : 4-*O*-methylene-D-glucitol (0·75 g.) {prepared by the method of Ness *et al.*[3] this compound had m. p. 163—164° and $[\alpha]_D^{17}$ −10·1° (*c* 2·10 in $H_2O$)} in dry pyridine (100 ml.) and the solution was kept at 0° for 15 min., and at room temperature for 3 hr. more before being poured into water. The precipitated solid recrystallized from ethanol, to give the 1 : 6-*dibenzoate* (0·62 g.), m. p. 155—156°, $[\alpha]_D^{15}$ +15·0° (*c* 2·14 in $CHCl_3$) (Found: C, 62·4; H, 5·2; Bz, 52·0. $C_{21}H_{22}O_8$ requires C, 62·7; H, 5·5; Bz, 52·2%).

*Acetylation of* 1 : 6-*Di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—This compound (0·30 g.), acetylated with acetic anhydride in pyridine, gave 3 : 5-di-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·33 g.), m. p. 185° (from ethanol) alone and on admixture with the specimen obtained previously.

3-O-*Acetoxymethyl*-5-O-*acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—(*a*) Prepared by the method of Hann, Wolfe, and Hudson [4] this compound had m. p. 125°, $[\alpha]_D^{22}$ +1·9° (*c* 2·18 in $CHCl_3$) (Found: C, 60·5; H, 5·3%; N-alkali uptake, 7·83 ml./g. Calc. for $C_{26}H_{28}O_{11}$: C, 60·5; H, 5·5%; N-alkali uptake, 7·75 ml./g.). These authors gave m. p. 115—116° and $[\alpha]_D^{20}$ +9·3° (in $CHCl_3$). (*b*) 1 : 6-Di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol (0·50 g.) was dissolved in warm trifluoroacetic anhydride (1·50 ml., 9 mol.) and acetic acid (6·21 ml., 90 mol.) and the solution was kept at 25° for 12 hr. Volatile material was then removed *in vacuo*, and the residual solid recrystallized from ethanol, to give 3-*O*-acetoxymethyl-5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·56 g.), m. p. 125° [alone and on admixture with the compound obtained as in (*a*)], $[\alpha]_D^{19}$ +2·4° (*c* 2·34 in $CHCl_3$) (Found: C, 60·6; H, 5·3%; N-alkali uptake, 7·51 ml./g.).

*Hydrolysis of* 3-O-*Acetoxymethyl*-5-O-*acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—The compound (1·50 g.) was dissolved in 2N-hydrochloric acid (2·0 ml.) and ethanol (5 ml.),

refluxed for 15 min., then cooled quickly. The precipitate was filtered off, washed with water, and recrystallized four times from ethanol, to give 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·38 g.), m. p. 147—149°, alone and on admixture with the compound obtained previously.

5-O-*Acetyl*-1 : 6-*di*-O-*benzoyl*-3-O-*methyl*-2 : 4-O-*methylene*-D-*glucitol*.—5-*O*-Acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (1·40 g.) was refluxed with silver oxide (5·0 g.) in methyl iodide (30 ml.) for 36 hr. The methyl iodide was removed and the residue extracted exhaustively with boiling chloroform. Evaporation of the filtered extracts left a syrup, which, when crystallized three times from ethanol, gave the 3-*methyl ether* (0·78 g.), m. p. 141—142°, depressed on admixture with the starting material, $[\alpha]_D^{19}$ +4·4° (*c* 1·54 in $CHCl_3$) (Found: C, 63·2; H, 5·7; OMe, 7·1%; N-alkali uptake, 6·45 ml./g. $C_{34}H_{36}O_9$ requires C, 62·9; H, 5·7; OMe, 6·8%; N-alkali uptake, 6·55 ml./g.).

3-O-*Methyl*-2 : 4-O-*methylene*-D-*glucitol*.—5-*O*-Acetyl-1 : 6-di-*O*-benzoyl-3-*O*-methyl-2 : 4-*O*-methylene-D-glucitol (0·40 g.) was kept in dry methanol (20 ml.), in which a small piece of sodium had been dissolved, at room temperature for 16 hr. Evaporation left a syrup which was sublimed at 150°/0·005 mm., to give a crystalline product. In a later experiment these crystals were used to seed the product from its solution in ethanol–ether, to give 3-O-*methyl*-2 : 4-O-*methylene*-D-*glucitol* (0·11 g.), m. p. 144°, depressed on admixture with the starting material, $[\alpha]_D^{21}$ −3·3° (*c* 2·70 in $H_2O$) (Found: C, 46·3; H, 7·4; OMe, 15·2. $C_8H_{14}O_6$ requires C, 46·2; H, 7·7; OMe, 14·9%).

Periodate oxidation by Reeves's method [22] showed that, after 20 min., 1 hr., and 17 hr., 1 mole of this compound had consumed 0·91, 0·97, and 1·04 moles of sodium periodate, respectively, and after 17 hr. had liberated 0·92 mole of formaldehyde, isolated as its dimedone derivative, m. p. and mixed m. p. 188°.

*Benzoylation of* 5-O-*Acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—(*a*) Attempted benzoylation with benzoyl chloride in pyridine was unsuccessful; the starting material was recovered in 80% yield together with a small amount of crystals with m. p. 141—142°, depressed on admixture with the starting material. (*b*) A solution of 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·18 g.) and benzoic acid (0·074 g., 1·50 mol.) in trifluoroacetic anhydride (0·084 ml., 1·50 mol.) and trifluoroacetic acid (0·20 ml.) was kept at 60° for 2 hr., poured into aqueous sodium hydrogen carbonate, and extracted with chloroform. The extracts were dried ($MgSO_4$) and evaporated to a syrup, which was twice crystallized from aqueous ethanol, to give 5-O-*acetyl*-1 : 3 : 6-*tri*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol* (0·15 g.), m. p. 142—142·5°, alone and on admixture with the compound obtained as in (*a*), depressed on admixture with the starting material, $[\alpha]_D^{17}$ −18·8° (*c* 1·60 in $CHCl_3$) (Found: C, 65·7; H, 5·1%; N-alkali uptake, 7·37 ml./g. $C_{30}H_{28}O_{10}$ requires C, 65·7; H, 5·1%; N-alkali uptake, 7·30 ml./g.).

1 : 5 : 6-*Tri*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—A solution of 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol (1·00 g.) and benzoic acid (2·65 g., 9 mol.) in trifluoroacetic anhydride (3·00 ml., 9 mol.) was kept at 25° for 12 hr., poured into aqueous sodium hydrogen carbonate, and extracted with chloroform. Evaporation of the dried ($MgSO_4$) extracts left a solid, which recrystallized from aqueous ethanol to give the 1 : 5 : 6-tribenzoate (0·78 g.), m. p. 154—154·5°, alone and on admixture with the tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol obtained by Bourne and Wiggins,[17] $[\alpha]_D^{15}$ −9·3° (*c* 3·33 in $CHCl_3$) (Found: C, 66·5; H, 4·9; Bz, 62·7. Calc. for $C_{30}H_{28}O_9$: C, 66·4; H, 5·2; Bz, 62·25%). Bourne and Wiggins gave m. p. 154° and $[\alpha]_D$ −10·0° (in $CHCl_3$).

3-O-*Acetyl*-1 : 5 : 6-*tri*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—1 : 5 : 6-Tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·40 g.) with acetic anhydride in pyridine gave the 3-*acetate*, needles (from ethanol) (0·44 g.), m. p. 107° (depressed on admixture with the 5-acetate obtained previously), $[\alpha]_D^{17}$ −12·8° (*c* 4·91 in $CHCl_3$) (Found: C, 65·7; H, 4·9%; N-alkali uptake 7·27 ml./g. $C_{32}H_{30}O_{10}$ requires C, 65·7; H, 5·1%; N-alkali uptake 7·30 ml./g.).

The authors thank Professor M. Stacey, F.R.S., for his interest and the University of Birmingham for the award of a Research Scholarship (to J. B.).

CHEMISTRY DEPARTMENT, THE UNIVERSITY, EDGBASTON, BIRMINGHAM, 15.
ROYAL HOLLOWAY COLLEGE, UNIVERSITY OF LONDON,
ENGLEFIELD GREEN, SURREY. [*Received, November 5th*, 1957.]

[22] Reeves, *J. Amer. Chem. Soc.*, 1941, **63**, 1476.

XUM

## 252. 1 : 2 : 3 : 4 : 5 : 6- *and* 1 : 2 : 3 : 4 : 5 : 7-*Hexamethylnaphthalene.*

By W. Carruthers and J. D. Gray.

The two hexamethylnaphthalenes named in the title have been synthesised. The "1 : 2 : 3 : 4 : 5 : 6"-hexamethylnaphthalene prepared by Abadir, Cook, and Gibson [2] is shown to be the 1 : 2 : 3 : 4 : 5 : 7-isomer. Treatment of 3-methyl-5-(2 : 3 : 4 : 5-tetramethylphenyl)hexan-2-one with hot polyphosphoric acid affords 1 : 2 : 3 : 4 : 6 : 7-hexamethylnaphthalene and an oil which appears to consist mainly of a derivative of indene.

Until recently very few polysubstituted naphthalene derivatives were known, but lately Mosby [1] and Abadir, Cook, and Gibson [2] have synthesised a number of polymethyl derivatives, including the octamethyl compound which was shown to be non-planar by Donaldson and Robertson [3] by *X*-ray crystallographic analysis. We have obtained the two hexamethylnaphthalenes named above in the course of unsuccessful attempts to prepare derivatives of octamethylnaphthalene suitable for optical resolution.

Reaction of prehnitene (1 : 2 : 3 : 4-tetramethylbenzene) with ethyl 2-methylpent-4-enoate in presence of aluminium chloride, after the method of Colonge and Grimaud,[4] afforded the ester (I) and hence, by hydrolysis and cyclisation of the acid chloride with stannic chloride, the hexamethyltetralone (II). This was smoothly converted into 1 : 2 : 3 : 4 : 5 : 7-hexamethylnaphthalene (III), m. p. 78—80°, by Clemmensen reduction and dehydrogenation of the tetrahydronaphthalene by palladium, or, better, by successive treatment with lithium aluminium hydride, potassium hydrogen sulphate, and palladium in boiling trichlorobenzene.

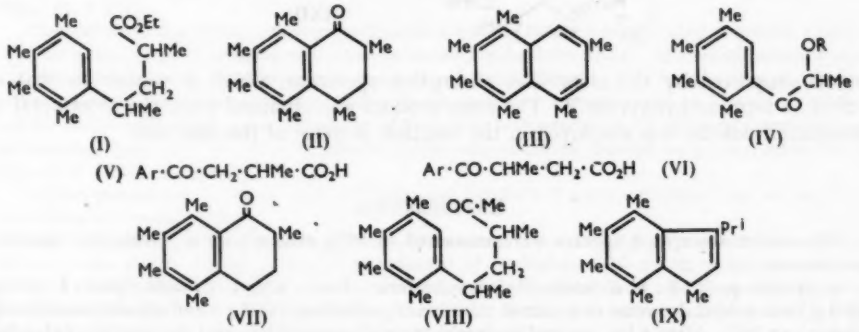
A hexamethylnaphthalene regarded as the 1 : 2 : 3 : 4 : 5 : 7-isomer has already been described by Abadir, Cook, and Gibson [2] who, however, recorded m. p. 140°; another hydrocarbon, m. p. 80°, was considered to be 1 : 2 : 3 : 4 : 5 : 6-hexamethylnaphthalene. We find that the latter is identical with our 1 : 2 : 3 : 4 : 5 : 7-isomer. The infrared spectra were superposable, and there was no depression of m. p. on admixture of our hydrocarbon and several of its derivatives with the original specimens, which were kindly put at our disposal by Dr. Cook. In conformity with the behaviour of other polyalkylnaphthalenes, our 1 : 2 : 3 : 4 : 5 : 7-hexamethylnaphthalene underwent a Diels–Alder reaction with maleic anhydride in hot benzene.[2,5] The adduct was oxidised by alkaline potassium permanganate to benzene-1 : 2 : 3 : 5-tetracarboxylic acid and this series of reactions proves the orientation of the methyl groups. The adduct of 1 : 2 : 3 : 4 : 5 : 6-hexamethylnaphthalene would have afforded benzene-1 : 2 : 3 : 4-tetracarboxylic acid on oxidation. In addition, we synthesised 1 : 2 : 3 : 4 : 5 : 6-hexamethylnaphthalene by standard procedures from ω-bromoacetylprehnitene and diethyl methylmalonate and showed that, in fact, it had m. p. 48—50°. An attempt to prepare the 1 : 2 : 3 : 4 : 5 : 7-isomer by a similar route failed because α-bromopropionylprehnitene and diethyl malonate in methanolic or ethanolic sodium alkoxide afforded only the α-ketol ethers (IV; R = Me or Et), while with diethyl sodiomalonate in benzene no reaction took place.

Abadir, Cook, and Gibson [2] prepared their supposed 1 : 2 : 3 : 4 : 5 : 6-hexamethylnaphthalene from the acid obtained in high yield by Friedel–Crafts reaction of prehnitene and methylsuccinic anhydride in ethylene chloride solution. This acid was regarded by them as the α-methyl acid (V; Ar = $C_6HMe_4$), but clearly to account for the formation of 1 : 2 : 3 : 4 : 5 : 7-hexamethylnaphthalene in the subsequent reactions, it must, in fact,

[1] Mosby, *J. Amer. Chem. Soc.*, 1952, **74**, 2564.
[2] Abadir, Cook, and Gibson, *J.*, 1953, 8.
[3] Donaldson and Robertson, *ibid.*, p. 17.
[4] Colonge and Grimaud, *Bull. Soc. chim. France*, 1951, 439, 857.
[5] Kloetzel, Dayton, and Herzog, *J. Amer. Chem. Soc.*, 1950, **72**, 273; Kloetzel and Herzog, *ibid.*, p. 1991.

be the β-methyl isomer (VI; Ar = $C_6HMe_4$). This is supported by the fact that the corresponding butyric acid is not identical with the α-methylbutyric acid which we synthesised. Friedel–Crafts reactions with methylsuccinic anhydride and aromatic hydrocarbons in nitrobenzene solution are generally held to give rise to the α-methyl-acid (V) in preponderant amount,[6] but it seems to be the case that different proportions of the two possible isomers are obtained when, instead, methylene or ethylene chloride is employed as solvent.[7] We confirmed that reaction of prehnitene and methylsuccinic anhydride in ethylene chloride led to the acid (VI; Ar = $C_6HMe_4$) almost exclusively; in nitrobenzene solution, on the other hand, a mixture was obtained from which the isomer (V) was isolated in moderate yield.

Attempts to convert the tetralone (II) into the unknown 1 : 2 : 3 : 4 : 5 : 6 : 8-heptamethylnaphthalene by reaction with methylmagnesium iodide or methyl-lithium were unsuccessful. The ketone was always recovered, even when reaction was continued for 40 hr. in boiling xylene or di-*n*-butyl ether. The complete resistance to reaction contrasts with the behaviour of the analogue (VII) and may possibly be ascribed to the " buttressing effect " [8] of the 4-methyl group of the ketone (II).




In other experiments, the ketone (VIII), obtained from prehnitene and 3-methylhex-5-en-2-one [9] in presence of aluminium chloride, was treated with polyphosphoric acid at 125—130°. An oily mixture was produced, from which a naphthalene hydrocarbon, m. p. 143—144°, was obtained directly in 30% yield. This was not the expected 1 : 2 : 3 : 4 : 5 : 6 : 8-heptamethyl derivative, however; it was identified as 1 : 2 : 3 : 4 : 6 : 7-hexamethylnaphthalene by mixed m. p.s of the hydrocarbon and of three derivatives with authentic specimens.[2] The formation of the hexamethylnaphthalene from the ketone (VIII) requires migration of one methyl group and elimination of another, and it seems likely that these processes take place after the formation of the highly sterically hindered heptamethyl compound. Migration of alkyl groups attached to the benzene ring in presence of hot polyphosphoric acid has already been noted by Mosby.[1,10] The remaining oily part of the reaction product was unsaturated. On oxidation with nitric acid it afforded mellitic acid, and this showed that it was a product of cyclisation, but it could not be dehydrogenated to a naphthalene derivative by palladium or with selenium. This fact, together with the ultraviolet absorption spectrum, which closely resembles that of indene,[11] suggests that the oil consists largely of one or more derivatives of indene (for example, IX), which may be envisaged as arising by rearrangement in the protonated ketone (VIII). The elementary analysis of the oil, and the somewhat reduced

[6] Berliner, " Organic Reactions," John Wiley & Sons, Inc., New York, 1949, Vol. V, p. 242.
[7] Baddar, Fahim, and Fleifel, *J.*, 1955, 2199.
[8] Westheimer and Reiger, *J. Amer. Chem. Soc.*, 1950, **72**, 19; Chien and Adams, *ibid.*, 1934, **56**, 1787.
[9] Colonge and Pichat, *Bull. Soc. chim. France*, 1941, 853, 855.
[10] Mosby, *J. Org. Chem.*, 1953, **18**, 485.
[11] Morton and de Gouveia, *J.*, 1934, 911.

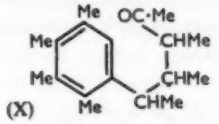


XUM

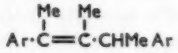
intensity of ultraviolet absorption, indicate that the corresponding indanes are also present, probably produced from the indenes by hydrogen transfer [12] involved in the formation of the hexamethylnaphthalene.

In another approach reduction of the ketone (VIII) with lithium aluminium hydride and treatment of the alcohol with concentrated sulphuric acid gave a liquid hydrocarbon which was not converted into a naphthalene by palladium or with selenium.

Before the nature of the product formed on cyclisation of ketone (VIII) was recognised, an attempt was made to prepare the homologue (X) (and thence possibly octamethylnaphthalene) by way of the reaction of 3-methylpentane-2 : 4-dione with the Grignard reagent or lithio-compound prepared from 1-prehnitylethyl bromide. The only product isolated was the hydrocarbon (XI; Ar = $C_6HMe_4$), formed by cleavage of the diketone and reaction with two molecules of the organometallic compound. The structure (XI) is assigned on analogy with similar recorded reactions of β-diketones with Grignard reagents,[13]




(X)




(XI)

and is supported by the ultraviolet absorption spectrum, which is similar to that of α-2 : 4 : 6-tetramethylstyrene.[14] The same product was obtained when the monoketal or monohemithioketal was employed in the reaction in place of the diketone.

## Experimental

Ultraviolet absorption spectra were measured in 95% ethanol, on a " Unicam " spectrophotometer.

*α-Methyl-γ-(2 : 3 : 4 : 5-tetramethylphenyl)valeric Acid.*—Ethyl 2-methylpent-4-enoate (45·3 g.) was added dropwise to a stirred mixture of prehnitene (45·6 g.) and aluminium chloride (64·5 g.) at 35°. After 4 hr., ice and hydrochloric acid were added, and the mixture extracted with ether. The *valerate* (77·6 g.) obtained had b. p. 198—200°/23 mm. (Found: C, 78·4; H, 10·0. $C_{18}H_{28}O_2$ requires C, 78·2; H, 10·2%).

The ester (77·6 g.) was hydrolysed by potassium hydroxide (20 g.) in boiling aqueous ethanol (200 c.c., 1 : 1) for 5 hr. The *acid* (70 g.) had m. p. 76—90° (Found: C, 77·2; H, 9·8. $C_{16}H_{24}O_2$ requires C, 77·4; H, 9·7%). Oxidation of the acid (200 mg.) with concentrated nitric acid (1·5 c.c.) and water (3 c.c.) at 175—180° for 6 hr. gave benzenepentacarboxylic acid, identified by conversion into the pentamethyl ester, m. p. and mixed m. p. 143—146°.

1 : 2 : 3 : 4-*Tetrahydro*-2 : 4 : 5 : 6 : 7 : 8-*hexamethyl*-1-*oxonaphthalene*.—A mixture of the foregoing acid (53 g.) and phosphorus pentachloride (47·7 g.) in benzene (220 c.c.) was kept at room temperature for 1 hr., then heated on the steam-bath for 5 min. The solution was cooled to 0° and stannic chloride (52 c.c.) in benzene (52 c.c.) added dropwise with stirring. After ½ hr. the mixture was decomposed with ice and hydrochloric acid, and the benzene layer separated and washed with sodium hydroxide and water. The *tetralone* distilled as a colourless oil at 212°/26 mm. (39 g.) and crystallised from methanol in colourless prisms, m. p. 62—63° (Found: C, 83·4; H, 9·5. $C_{16}H_{22}O_2$ requires C, 83·4; H, 9·6%). The ketone did not react with semicarbazide acetate, but slowly formed a 2 : 4-*dinitrophenylhydrazone*, orange-red needles, m. p. 167—168° (Found: N, 13·9. $C_{22}H_{26}O_4N_4$ requires N, 13·7%).

1 : 2 : 3 : 4 : 5 : 7-*Hexamethylnaphthalene*.—(*a*) The above ketone (1 g.) was reduced with lithium aluminium hydride (0·17 g.) in refluxing ether for 2 hr. Next morning the alcohol (0·93 g.) was isolated in the usual way, and dehydrated by fused potassium hydrogen sulphate (90 mg.) at 160° for 10 min. The product was distilled and the dihydronaphthalene (0·74 g.) obtained as crystals, m. p. 38—39°. This material (0·33 g.) was dehydrogenated with 20%

[12] Cf. Gutsche, Saha, and Johnson, *J. Amer. Chem. Soc.*, 1957, **79**, 4441.
[13] Kohler and Erickson, *ibid.*, 1931, **53**, 2301.
[14] Newman and Deno, *ibid.*, 1951, **73**, 3644.

palladium–charcoal in boiling trichlorobenzene under carbon dioxide for 5 hr. 1 : 2 : 3 : 4 : 5 : 7-*Hexamethylnaphthalene* (0·19 g.) was obtained as colourless plates (from *cyclo*hexane), m. p. 78—80° (Found: C, 90·4; H, 9·5. $C_{16}H_{20}$ requires C, 90·6; H, 9·4%). The *picrate* formed red needles, m. p. 169—170° (Found: N, 9·4. $C_{16}H_{20}.C_6H_3O_7N_3$ requires N, 9·5%), and the 2 : 4 : 7-trinitrofluorenone complex deep red needles, m. p. 181—182° (from benzene).

(*b*) The foregoing ketone (0·32 g.) and amalgamated zinc (1 g.) were boiled with hydrochloric acid (1·8 c.c.), water (0·75 c.c.), and toluene (1 c.c.) for 24 hr. The cooled mixture was extracted with benzene, and the recovered tetrahydronaphthalene (0·24 g.) dehydrogenated directly by 30% palladium–charcoal (0·1 g.) at about 325° for 2 hr. in an atmosphere of carbon dioxide. The resulting 1 : 2 : 3 : 4 : 5 : 7-hexamethylnaphthalene (0·19 g.), purified through its picrate, crystallised from *cyclo*hexane as colourless plates, m. p. 78—80°, not depressed when mixed with the hydrocarbon obtained as above.

*Maleic Anhydride Adduct of* 1 : 2 : 3 : 4 : 5 : 7-*Hexamethylnaphthalene.*—A solution of the hydrocarbon (1·6 g.) and freshly distilled maleic anhydride (24 g.) in benzene (32 c.c.) was boiled for 48 hr., and benzene removed under reduced pressure. The residue was worked up by the method of Kloetzel, Dayton, and Herzog,[5] and the crude adduct acid reconverted into the *adduct* anhydride by crystallisation from ethyl acetate containing a few drops of acetic anhydride, giving colourless crystals (1·6 g.), m. p. 147° (Found: C, 77·5; H, 6·8. $C_{20}H_{22}O_3$ requires C, 77·4; H, 7·2%).

The adduct (1·6 g.) in 1% sodium hydroxide solution (100 c.c.) was treated dropwise with 8% aqueous potassium permanganate (excess) on the steam-bath for 16 hr. Excess of permanganate was decomposed with methanol, and the hot solution filtered. The residue was thoroughly extracted with hot water, and the combined filtrates were concentrated to 150 c.c., acidified, and extracted with ether. On treatment of the crude acid product with ethereal diazomethane, tetramethyl benzene-1 : 2 : 3 : 5-tetracarboxylate was obtained, having m. p. and mixed m. p. 109—111° (from methanol).

5-*Acetylprehnitene.*—The method of Claus and Föhlisch [15] gave a mixture and we employed the following modification.

A solution of acetyl chloride (6·3 g.) and aluminium chloride (10·1 g.) in methylene chloride (20 c.c.) was slowly added to a stirred solution of prehnitene (10 g.) in methylene chloride (20 c.c.) at 0°. After 1 hr. at room temperature, ice and hydrochloric acid were added and the methylene chloride layer was separated and washed. 5-*Acetylprehnitene* had b. p. 135°/5 mm., $n_D^{19}$ 1·5437 (Found: C, 81·7; H, 8·8. $C_{12}H_{16}O$ requires C, 81·8; H, 9·2%). The 2 : 4-*dinitrophenylhydrazone* formed orange-red needles, m. p. 178—179° (Found: C, 61·1; H, 5·7. $C_{18}H_{20}O_4N_4$ requires C, 60·7; H, 5·7%). The semicarbazone had m. p. 210—211° (lit., 209°).

Oxidation of acetylprehnitene with sodium hypoiodite [16] afforded prehnitic acid, m. p. 165—169° (lit., 165°, 169°), which when heated with soda-lime was reconverted into prehnitene, identified by comparison of its infrared spectrum with that of an authentic specimen.

ω-*Bromoacetylprehnitene.*—A solution of bromine (8·6 g.) in carbon tetrachloride (30 c.c.) was slowly added at room temperature to a stirred solution of 5-acetylprehnitene (9·5 g.) in carbon tetrachloride (20 c.c.). Then the solution was kept for ½ hr. and washed with sodium carbonate solution and with water. The crude product distilled at 148—150°/1·5 mm., and solidified (13 g.). Crystallisation from light petroleum (b. p. 40—60°) gave ω-*bromoacetylprehnitene*, m. p. 54—55° (Found: C, 56·8; H, 5·9. $C_{12}H_{15}OBr$ requires C, 51·8; H, 5·9%). Oxidation of the compound with sodium hypobromite gave prehnitic acid, m. p. 170°.

α-*Methyl-γ-oxo-γ-*(2 : 3 : 4 : 5-*tetramethylphenyl*)*butyric Acid.*—α-Bromoacetylprehnitene (13 g.) in ethanol (15 c.c.) was gradually added at 60° to a stirred solution prepared from sodium (1·3 g.) and diethyl methylmalonate (8·9 g.) in ethanol. After 2 hr. most of the ethanol was removed on the steam-bath, water was added, and the mixture was extracted with ether. The washed and dried solution was evaporated, and the product distilled as a colourless oil (9·1 g.) at 172°/0·3 mm. This was hydrolysed with potassium hydroxide (5·1 g.) in 1 : 1 aqueous ethanol (50 c.c.), and the resulting malonic acid was decarboxylated at 180° (until evolution of carbon dioxide ceased). The crude *acid* was distilled and crystallised from benzene–light petroleum (b. p. 40—60°) in blades, m. p. 129—130° (Found: C, 72·6; H, 7·95. $C_{15}H_{20}O_3$ requires C, 72·55; H, 8·1%).

α-*Methyl-γ-*(2 : 3 : 4 : 5-*tetramethylphenyl*)*butyric Acid.*—A solution of the above keto-acid

[15] Claus and Föhlisch, *J. prakt. Chem.*, 1888, **38**, 230.
[16] Fuson and Tullock, *J. Amer. Chem. Soc.*, 1934, **56**, 1638.

XUM

(1·5 g.), sodium hydroxide (0·9 g.), and 90% hydrazine hydrate (0·9 c.c.) in diethylene glycol (20 c.c.) was boiled for ½ hr. The temperature was then raised to 200° by distilling off water, and boiling continued 4 hr. The cooled mixture was poured into water and acidified, and the product extracted with ethyl acetate. The *butyric acid* (1·2 g.) obtained had m. p. 77—78° [from light petroleum (b. p. 40—60°)] (Found: C, 77·1; H, 9·2. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·5%).

**1 : 2 : 3 : 4-***Tetrahydro***-2 : 5 : 6 : 7 : 8-***pentamethyl***-1-***oxo-naphthalene*.—The foregoing butyric acid (0·9 g.) was cyclised as described above for a similar case, using phosphorus pentachloride (0·84 g.) and stannic chloride (0·9 c.c.). The *product* crystallised from light petroleum in prisms, m. p. 57—58° (Found: C, 83·5; H, 9·2. $C_{15}H_{20}O_2$ requires C, 83·3; H, 9·3%).

**1 : 2-***Dihydro***-3 : 4 : 5 : 6 : 7 : 8-***hexamethylnaphthalene*.—A solution of the preceding ketone (0·56 g.) in ether (5 c.c.) was added under nitrogen to a stirred solution of methyl-lithium, prepared from methyl iodide (7 g.) and lithium (0·7 g.). After 6 hr. most of the ether was removed, benzene (20 c.c.) was added, and the mixture boiled for 3 hr. The cooled mixture was poured on ice and hydrochloric acid, and the product isolated in the usual way. The *dihydronaphthalene* was obtained as crystals, m. p. 89—90°, from ethanol (Found: C, 89·5; H, 10·4. $C_{16}H_{22}$ requires C, 89·65; H, 10·35%).

**1 : 2 : 3 : 4 : 5 : 6-***Hexamethylnaphthalene*.—The dihydronaphthalene described above (0·11 g.) and 30% palladium–charcoal (0·6 g.) were heated in boiling trichlorobenzene in an atmosphere of carbon dioxide. Evolution of hydrogen was very slow, and after 17 hr. was not complete. The product was isolated through its picrate and distilled. It separated from methanol as a colourless microcrystalline powder (60 mg.), m. p. 48—50° (Found: C, 90·2; H, 9·4. $C_{16}H_{20}$ requires C, 90·6; H, 9·4%), $\lambda_{max.}$ 241, 301, 337 mμ (log ε 4·82, 3·68, 2·74). The *s-trinitrobenzene complex* formed yellow needles, m. p. 186—189° (Found: C, 62·4; H, 5·3. $C_{16}H_{20}.C_6H_3O_6N_3$ requires C, 62·2; H, 5·5%). The picrate, m. p. 155—157°, was unstable.

*5-Propionylprehnitene*.—This *ketone* was prepared from prehnitene (5 g.), propionyl chloride (3·5 g.), and aluminium chloride (5 g.) in methylene chloride as described above for acetylprehnitene. It (7 g.) had b. p. 104°/0·2 mm., $n_D^{22}$ 1·5345 (Found: C, 82·1; H, 9·2. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%).

*α-Bromo-5-propionylprehnitene*.—This was prepared from 5-propionylprehnitene (6·4 g.) and bromine (5·4 g.) in carbon tetrachloride as described for α-bromoacetylprehnitene. The *bromo-compound* (7·7 g.) crystallised from light petroleum (b. p. 40—60°) in colourless plates, m. p. 36·5—37·5° (Found: 57·9; H, 6·6. $C_{13}H_{17}OBr$ requires C, 58·0; H, 6·4%). On oxidation with sodium hypobromite it gave prehnitic acid, m. p. 165—169°.

*Reaction of α-Bromo-5-propionylprehnitene and Diethyl Malonate*.—Diethyl malonate (4·6 g.) was added to a solution of sodium ethoxide prepared from sodium (0·66 g.) and ethanol (15 c.c.), and to the resulting solution α-bromo-5-propionylprehnitene (7·7 g.) in ethanol (10 c.c.) was added at 60°. After 2 hr. most of the ethanol was distilled off and the product isolated in the usual way. The *ketol ether* (6·4 g.) obtained had b. p. 104—110°/0·1 mm. (Found: C, 76·2; H, 8·9. $C_{15}H_{22}O_3$ requires C, 76·9; H, 9·5%). This product reduced Fehling's solution, and on treatment with boiling aqueous-alcoholic potassium hydroxide afforded prehnitic acid, m. p. and mixed m. p. 165—169°.

*Reaction of Prehnitene and Methylsuccinic Anhydride*.—(*a*) Methylsuccinic anhydride (4·3 g.) and aluminium chloride (10 g.) in nitrobenzene (30 c.c.) were gradually added to a stirred solution of prehnitene (5 g.) in nitrobenzene (5 c.c.) at 0°. The mixture was kept at room temperature for 1 hr., then ice and hydrochloric acid were added and the nitrobenzene was steam-distilled. A mixture of acids was obtained, from which α-methyl-γ-oxo-γ-(2 : 3 : 4 : 5-tetramethylphenyl)butyric acid (2 g.), m. p. 130—131°, was isolated by crystallisation from methanol and from benzene–light petroleum (b. p. 40—60°). The m. p. was not depressed on admixture with the acid prepared as described above. No other pure component was isolated from the residual mixture.

(*b*) Reaction in ethylene chloride solution, as described by Abadir, Cook, and Gibson,[2] gave β-methyl-γ-oxo-γ-(2 : 3 : 4 : 5-tetramethylphenyl)butyric acid exclusively in 85% yield. In our hands, the pure acid, recovered from the ethyl ester, had m. p. 112° (lit., 131°). On reduction by the Clemmensen method it furnished the butyric acid, m. p. 106—107° (lit., 106—107°).

*Condensation of Prehnitene and* **3-***Methylhex***-5-***en***-2-***one*.—This ketone (7·3 g.) was added dropwise to a stirred mixture of prehnitene (8·2 g.) and powdered aluminium chloride (12·8 g.) at 35°. After 4 hr. the complex was decomposed with ice and hydrochloric acid, and the organic layer was extracted with ether. **3-***Methyl***-5-(2 : 3 : 4 : 5-***tetramethylphenyl***)***hexan***-2-***one***

(11·2 g.) was obtained as a colourless oil, b. p. 159°/3 mm., $n_D^{19}$ 1·5188 (Found: C, 82·9; H, 10·3. $C_{17}H_{26}O$ requires C, 82·9; H, 10·6%). The *semicarbazone* had m. p. 183—184° (Found: C, 71·3; H, 9·5. $C_{18}H_{29}ON_3$ requires C, 71·3; H, 9·6%). Oxidation with concentrated nitric acid at 175—180° gave benzenepentacarboxylic acid, identified by comparison of the pentamethyl ester, m. p. 144—146°, with an authentic specimen.

3-*Methyl*-5-(2 : 3 : 4 : 5-*tetramethylphenyl*)*hexan*-2-*ol*.—A solution of the hexanone (2 g.) in ether (10 c.c.) was added dropwise to a slurry of lithium aluminium hydride (0·31 g.) in ether. The mixture was boiled for 2 hr., and excess of hydride was then decomposed with ethyl acetate. The *product*, worked up in the usual way, had b. p. 112°/0·07 mm. (Found: C, 82·5; H, 11·0. $C_{17}H_{28}O$ requires C, 82·2; H, 11·4%).

When this alcohol (1·5 g.) was added with stirring to concentrated sulphuric acid (2 g.) at 10°, and the mixture stirred at room temperature for 3 hr., the *product* obtained by addition of ice, was an oil, b. p. 122—123°, with no hydroxyl maximum in the infrared spectrum (Found: C, 88·4; H, 9·8. $C_{17}H_{26}$ requires C, 88·7; H, 11·3%).

*Reaction of* 3-*Methyl*-5-(2 : 3 : 4 : 5-*tetramethylphenyl*)*hexan*-2-*one with Polyphosphoric Acid*.—The foregoing ketone (11·2 g.) was added dropwise, at room temperature, to stirred polyphosphoric acid prepared from phosphoric oxide (125 g.) and concentrated phosphoric acid (50 c.c.), and the mixture was then heated at 125—130° for 5 hr., with occasional stirring. The cooled mixture was diluted with ice-water, and the organic material was extracted with ether. The product was distilled and two fractions were collected at 100—103°/0·07 mm. (4·2 g.) and 125—130°/0·07 mm. (3·2 g.). The second fraction solidified, and after crystallisation from benzene–light petroleum gave colourless plates of 1 : 2 : 3 : 4 : 6 : 7-hexamethylnaphthalene, m. p. and mixed m. p. 143—144° (Found: C, 90·4; H, 9·5. Calc. for $C_{16}H_{26}$: C, 90·5; H, 9·5%), $\lambda_{max.}$ 237, 293 mμ (log ε 4·90, 3·81). The dark red picrate had m. p. 194—195° (Found: C, 60·4; H, 5·7. Calc. for $C_{16}H_{26}.C_6H_3O_7N_3$: C, 60·1; H, 5·2%), and the 2 : 4 : 7-trinitrofluorenone complex, m. p. 205—206° (Found: C, 66·4; H, 4·7. Calc. for $C_{16}H_{26}.C_{13}H_5O_7N_3$: C, 66·1; H, 4·7%). Both m. p.s were undepressed on admixture with authentic specimens.

The first fraction above was redistilled and collected as a colourless oil at 140°/0·8 mm., $n_D^{25}$ 1·5441 (Found: C, 88·7; H, 11·0. Calc. for $C_{17}H_{26}$: C, 88·7; H, 11·3. Calc. for $C_{17}H_{24}$: C, 89·5; H, 10·5%), $\lambda_{max.}$ 220, 255,(295) mμ [log ε 4·24, 3·60, (2·96)]. The oil decolorised bromine water and potassium permanganate solution, and gave a yellow-brown colour with tetranitromethane. With dilute nitric acid at 175—180°, it gave benzenehexacarboxylic acid, m. p. and mixed m. p. 185—187°. It was recovered after being heated with selenium in a sealed tube at 310° for 100 hr.; at 360° (70 hr.) charring occurred.

5-1′-*Hydroxyethylprehnitene*.—5-Acetylprehnitene (18·5 g.) was added dropwise to a slurry of lithium aluminium hydride (4 g.) in ether (20 c.c.), and the mixture refluxed for 3 hr. The *alcohol* was isolated in the usual manner and had b. p. 121°/1 mm. (14 g.). It crystallised in light petroleum as prisms, m. p. 53—54° (Found: C, 81·2; H, 10·0. $C_{12}H_{18}O$ requires C, 80·9; H, 10·2%).

5-1′-*Bromoethylprehnitene*.—A solution of phosphorus tribromide (3·2 g.) in ether (250 c.c.) was added dropwise at −25° to a stirred solution of the above alcohol (5 g.) and pyridine (0·5 g.) in ether (250 c.c.). The mixture was then stirred at −25° for ½ hr. and next morning poured into ice water, and the ether layer was separated and washed with sodium hydrogen carbonate solution and with water. The crude *bromide* was distilled (b. p. 90°/0·05 mm.; 4·8 g.) and, crystallised from light petroleum (b. p. 40—60°), had m. p. 48° (Found: C, 60·1; H, 7·2. $C_{12}H_{17}Br$ requires C, 59·8; H, 7·1%).

In one experiment the crude bromide from 10·6 g. of alcohol was distilled at 120°/0·15 mm.; hydrogen bromide was evolved and, in addition to a small amount (1·8 g.) of bromide, a hydrocarbon (6·8 g.), b. p. 200°/0·15 mm., was obtained. This hydrocarbon crystallised from benzene in plates, m. p. 169—170°. Its ultraviolet absorption was very similar to that of 9 : 10-dihydroanthracene, and the hydrocarbon is possibly 9 : 10-*dihydro*-1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-*decamethylanthracene*, formed by condensation of two molecules of the bromide (Found: C, 90·2; H, 9·5. $C_{24}H_{32}$ requires C, 89·9; H, 10·1%). It had $\lambda_{max.}$ 230 (infl.), 272 (log ε 4·18, 3·24) and was recovered after being heated with selenium at 310°; at 340° for 50 hr. the product was charred.

*Reaction of* 1-(2 : 3 : 4 : 5-*Tetramethylphenyl*)*ethylmagnesium Bromide and* 3-*Methylpentane*-2 : 4-*dione*.—The solution prepared from the above bromide (0·49 g.) and magnesium (0·05 g.) in ether (20 c.c.) was added dropwise to a stirred solution of the dione (0·25 g.) in ether (20 c.c.)

XUM

at −80°. An immediate reaction took place and a complex was precipitated. After 4 hr. the suspension was added slowly to an ice-cold solution of ammonium chloride. The mixture was extracted with ether, and afforded *3-methyl-2 : 4-di-(2 : 3 : 4 : 5-tetramethylphenyl)pent-2-ene* (0·25 g.) as colourless prisms (from benzene), m. p. 220—223° (Found: C, 90·0; H, 10·2. $C_{26}H_{36}$ requires C, 89·6; H, 10·4%), $\lambda_{max.}$ (220), 270, 279 [log ε (4·48), 2·98, 2·94].

*Ethylene Monoketal and Ethylene Monohemithioketal of 3-Methylpentane-2 : 4-dione.*—A mixture of the dione (32 g.), ethylene glycol (18·5 g.), and toluene-*p*-sulphonic acid (100 mg.) in dry benzene (400 c.c.) was refluxed (20 hr.) until no more water separated. The *ketal* (25·6 g.) obtained had b. p. 60°/0·1 mm., $n_D^{20}$ 1·4411 (Found: C, 60·3; H, 9·0. $C_8H_{14}O_3$ requires C, 60·7; H, 8·9%).

The *hemithioketal* (17·3 g.), obtained in the same way from the dione (21 g.) and 2-mercaptoethanol (16 g.), had b. p. 56°/0·1 mm., $n_D^{23}$ 1·4860 (Found: C, 55·5; H, 8·4. $C_8H_{14}O_2S$ requires C, 55·2; H, 8·1%).

We are indebted to the Department of Scientific and Industrial Research for a maintenance allowance (to J. D. G.), and to Dr. J. W. Cook, F.R.S., for suggesting this investigation and for his interest in its progress. Microanalyses were by Mr. J. M. L. Cameron and Miss M. Christie.

University of Glasgow.
Medical Research Council, Carcinogenic Substances Research Group,
University of Exeter. [*Received, November 12th,* 1957.]

---

## 253. *Phenylation with Diazoaminobenzenes.*

By R. L. Hardie and R. H. Thomson.

Pyrolysis of diazoaminobenzene in aromatic solvents at 150—160° generates phenyl and anilino-radicals. The former attack the solvent, giving relatively high yields of diphenyl derivatives and negligible amounts of by-products. Three out of four unsymmetrical diazoaminobenzenes examined gave mixtures of amines and diphenyls which show that these triazens undergo decomposition in both tautomeric forms.

It is well known that diazoaminobenzenes decompose on being heated, with the evolution of nitrogen. This property has been exploited for the production of sponge rubber,[1] but little is known of the fate of the aromatic fragments although it is of interest that the reaction has also been used to initiate polymerisation.[2] Heating diazoaminobenzene at 150°, in sand or paraffin,[3] yields benzene, aniline, diphenyl, diphenylamine, and *o*- or *p*-aminodiphenyl, besides nitrogen, and decomposition in hot aniline [4,5] gives, in addition, azobenzene and aminoazobenzene. The latter procedure has been recommended for the preparation of the aminodiphenyls.[4,6] Similar products were obtained on pyrolysis of diazoaminotoluene in *p*-toluidine.[5] Although it is generally assumed [7] that these are homolytic decompositions there is very little direct evidence in the literature. Recent kinetic studies [8] show that radicals are formed on thermal dissociation of alkylaryltriazens

[1] Guppy, *Trans. Inst. Rubber Ind.*, 1942—3, **18**, 65.
[2] U.S.P. 2,313,233.
[3] Heusler, *Annalen*, 1890, **260**, 227.
[4] Hirsch, *Ber.*, 1892, **25**, 1973.
[5] Morgan and Walls, *J.*, 1930, 1502.
[6] Aeschlimann, Lees, McCleland, and Nicklin, *J.*, 1925, **127**, 66.
[7] Saunders, "The Aromatic Diazo Compounds," Arnold & Co., London, 2nd Edn., 1949, p. 175.
[8] Dolgoplosk, Ugryumov, and Krol, *Doklady Akad. Nauk S.S.S.R.*, 1954, **96**, 757; Dolgoplosk, Erusalimskii, Krol, and Romanov, *Zhur. obshchei Khim.*, 1954, **24**, 1775; Andakushkin, Dolgoplosk, and Radchenko, *ibid.*, 1956, **26**, 2972, 3403; Romanov, Dolgoplosk, and Erusalimskii, *Doklady Akad. Nauk S.S.S.R.*, 1957, **112**, 703.

and this is true, of course, in the presence of acid.[9] The present work establishes that diaryltriazens (diazoaminobenzenes) decompose homolytically when heated.

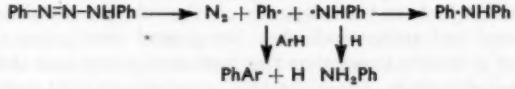
The decompositions were effected by heating 4% solutions of diazoaminobenzene in various aromatic solvents at 150—160° for 40 hr. During this time the initial light yellow solutions darkened appreciably but no tar separated (except from nitrobenzene solution). Primary amines were then removed by acid-extraction and the remaining mixture was fractionated by distillation and chromatography. The products isolated are set out in Table 1. Mixtures of isomeric diphenyls were formed in each case but complete separation was not achieved. Although 2-chlorodiphenyl was the only isomer isolated on pyrolysis of diazoaminobenzene in chlorobenzene, all three isomers were disclosed by infrared

TABLE 1. *Products isolated on pyrolysis of diazoaminobenzene in organic solvents.*

| Solvent | $Ph_2$ derivs. | Amines |
|---|---|---|
| Bromobenzenes | 2- and 4-Bromo- | $NH_2Ph$, $NHPh_2$ |
| Chlorobenzene | 2-Chloro- | $NH_2Ph$ |
| Nitrobenzene * | 2- and 4-Nitro- | $NH_2Ph$, $NHPh_2$ |
| *iso*Propylbenzene † | Mixed *iso*propyl- | ,, |

* Azobenzene was also isolated from this solvent. † 2 : 3-Dimethyl-2 : 3-diphenylbutane was also isolated from this solvent.

analysis,[10] and the isomer ratio is in general agreement with those obtained by other phenylation procedures (see Table 2). From this, and the formation of 2 : 3-dimethyl-2 : 3-diphenylbutane in the decomposition of diazoaminobenzene in *iso*propylbenzene, we conclude that the pyrolysis of diazoaminobenzene generates phenyl radicals which then attack the solvent. The reaction can be represented as follows:




no benzene was detected (cf. ref. 13). Thus, in the pyrolysis of diazoaminobenzene we have yet another method of phenylation. It has an advantage over other procedures in that the reactions are "clean," yields being relatively high (usually >50%) and the formation of by-products negligible. On the other hand, the method is not applicable to

TABLE 2. *Phenylation of chlorobenzene. Isomer ratios* (%).

| Method | *ortho* | *meta* | *para* |
|---|---|---|---|
| Gomberg [10] | 64·6 | 21·7 | 13·7 |
| Benzoyl peroxide [11] | 57·5 | 26·6 | 15·9 |
| Silver iodide dibenzoate [12] | 60·0 | 24·0 | 16·0 |
| Phenylhydrazine–silver oxide [13] | 64·9 | 22·1 | 13·0 |
| Phenylazotriphenylmethane [11] | 58·2 | 27·9 | 13·9 |
| Diazoaminobenzene | 59·8 | 23·7 | 16·5 |

TABLE 3. *Products obtained on pyrolysis of substituted diazoaminobenzenes in bromobenzene.*

| Diazoaminobenzene | $Ph_2$ derivs. | Amines |
|---|---|---|
| 4-Bromo- | 2- and 4-Bromo- | *p*-Bromoaniline and 4-bromodiphenylamine |
| 4 : 4′-Dibromo- | 2 : 4′-, 3 : 4′-, and 4 : 4′-Dibromo- | *p*-Bromoaniline |
| 4-Nitro- | Mixed bromo- and 2-bromo-4′-nitro- | *p*-Nitroaniline |
| 4-Bromo-4′-nitro- | 4 : 4′-Dibromo- and 2-bromo-4′-nitro- | *p*-Nitroaniline |
| 4-Methoxy- | Mixed bromo- and 2-, 3-, and 4-bromo-4′-methoxy- | Aniline and *p*-anisidine |

[9] Elks and Hey, *J.*, 1943, 441.
[10] Augood, Hey, and Williams, *J.*, 1953, 45.
[11] Huisgen and Grashey, *Annalen*, 1957, **607**, 46.
[12] Bryce-Smith and Clarke, *J.*, 1956, 2264.
[13] Hardie and Thomson, *J.*, 1957, 2512.

benzene and a few other low-boiling aromatic solvents. The only other symmetrical diazoaminobenzene examined was the 4 : 4′-dibromo-derivative: in boiling bromobenzene it yielded all three dibromodiphenyls and *p*-bromoaniline (see Table 3).

Since diazoaminobenzenes are tautomeric it would be expected that thermal dissociation of unsymmetrical derivatives would yield two different aryl radicals and two different arylamino-radicals, and so two groups of diphenyl derivatives and two primary amines. In three examples, out of four that we examined (all in bromobenzene), this proved to be the case (see Table 3). We did not succeed in isolating all the expected products but sufficient were obtained to show that both tautomeric forms were present in boiling bromobenzene. This provides novel evidence for the tautomerism of these com-

$$\begin{array}{l} \mathrm{Ar{-}N{=}N{-}NHAr'} \longrightarrow \mathrm{Ar\cdot} + \mathrm{N_2} + \mathrm{\cdot NHAr'} \\ \qquad\qquad \rightleftharpoons \\ \mathrm{ArNH{-}N{=}NAr'} \longrightarrow \mathrm{Ar'\cdot} + \mathrm{N_2} + \mathrm{\cdot NHAr} \end{array}$$

pounds. 4-Methoxydiazoaminobenzene gave the most satisfactory results and we were able to isolate a mixture of bromodiphenyls and all three bromo-4′-methoxydiphenyls, together with aniline and *p*-anisidine. From 4-nitro- and 4-bromo-4′-nitro-diazoaminobenzene we isolated at least one diphenyl derivative arising from each of the aryl radicals but only one base (*p*-nitroaniline); however the yield of bromonitrodiphenyl was very small, in both cases, so that the amounts of the second primary amine formed would be smaller still, and escaped detection. Judging from the products isolated, 4-bromodiazoaminobenzene reacts exclusively in one tautomeric form in boiling bromobenzene. The direction of thermal dissociation is presumably controlled by the combined energies of the two radicals liberated, which in turn depends on the relative stabilising influence of the substituents on phenyl and anilino-radicals. No general conclusions can be drawn from these few results but it is of interest that the methoxyl group had the least influence on the course of the decomposition, approximately equal amounts of aniline and *p*-anisidine being obtained (cf. ref. 14).

Benzotriazoles (cyclic triazens) are much more stable than diazoaminobenzenes and many can be distilled without decomposition at normal pressures. However, at very high temperatures, 1-aryl derivatives break up with loss of nitrogen; this must produce a diradical which then rearranges to a carbazole (Graebe's synthesis).

## Experimental

Solvents were fractionally distilled through a 50 cm. helix-packed column, and stored over sodium hydroxide pellets. *iso*Propylbenzene was purified by the method of Hey *et al.*[15] and had b. p. 152°/760 mm. Chromatographic separations were done on alumina with light petroleum (b. p. 50—60°) as solvent unless otherwise stated, and products were identified by mixed m. p. determinations.

*Pyrolysis of Diazoaminobenzenes in Aromatic Solvents.—General method.* A 4% solution of the diazoaminobenzene in an aromatic solvent was boiled under reflux for 40 hr. On cooling, the solution was extracted with dilute hydrochloric acid to obtain the amine(s), and then washed with a 5% solution of sodium hydrogen carbonate, and water, and dried ($MgSO_4$). The solvent was removed by distillation *in vacuo* through a helix-packed column, and the product worked up as indicated below.

*Diazoaminobenzene in bromobenzene.* From 20 g. of diazoaminobenzene, 5·7 g. of aniline were obtained. Distillation of the crude product gave a light red oil, b. p. 102—125°/0·3 mm., (15·5 g.). Chromatography gave (*a*) mixed bromodiphenyls, b. p. 96—105°/0·3 mm. (11·0 g.) (Found: C, 61·7; H, 4·05; Br, 34·3. Calc. for $C_{12}H_9Br$: C, 61·8; H, 3·85; Br, 34·3%), (*b*) 4-bromodiphenyl (1·8 g.), and (*c*) diphenylamine (0·4 g.). 2-Bromodiphenyl was isolated from (*a*) as its dinitro-derivative by treatment with ethyl nitrate in concentrated sulphuric acid, to give

[14] Huang and Si-Hoe, *J.*, 1957, 3988.
[15] Hey, Pengilly, and Williams, *J.*, 1956, 1466.

2-bromo-4′ : 5-dinitrodiphenyl, m. p. 163° (0·8 g.) (cf. ref. 16) (Found: C, 44·4; H, 2·15; N, 8·4. Calc. for $C_{12}H_7O_4N_2Br$: C, 44·5; H, 2·15; N, 8·6%).

*Diazoaminobenzene in chlorobenzene.* From 10 g. of diazoaminobenzene, 2·8 g. of aniline were obtained. Distillation of the product after removal of the solvent gave a light red oil, b. p. 102—110°/0·5 mm. (6·3 g.) (impure chlorodiphenyls). Purification of this oil for infrared analysis was effected by shaking it in light petroleum with concentrated sulphuric acid until all the colour had passed into the acid layer. The light petroleum solution was then washed with a 5% solution of sodium hydrogen carbonate, and water, and dried ($MgSO_4$). Removal of the solvent and distillation afforded mixed chlorodiphenyls, b. p. 95—102°/0·2 mm. (Found: C, 76·4; H, 4·7. Calc. for $C_{12}H_9Cl$: C, 76·4; H, 4·7%). Chromatography afforded 2-chlorodiphenyl, as a faintly yellow oil which crystallised from aqueous alcohol as prisms, m. p. 34°.

*Diazoaminobenzene in nitrobenzene.* The crude product from diazoaminobenzene (10 g.), after removal of aniline (2·6 g.), distilled to a light red oil, b. p. 120—145°/0·7 mm. (6·7 g.). Chromatography afforded (*a*) azobenzene (0·3 g.), (*b*) a light yellow oil (2·9 g.), crystallisation of which from aqueous alcohol gave 2-nitrodiphenyl, (*c*) 4-nitrodiphenyl (1·3 g.), and (*d*) diphenylamine (0·4 g.).

*Diazoaminobenzene in* iso*propylbenzene.* The crude product from 10 g. of diazoaminobenzene, after extraction of aniline (3 g.), distilled to give an orange oil, b. p. 110—145°/0·6 mm. (3·9 g.), chromatography of which afforded a diaryl fraction (3·2 g.). 2 : 3-Dimethyl-2 : 3-diphenylbutane (0·5 g.) was precipitated from this oil by nitromethane.[14] Mixed *iso*propyldiphenyls were obtained from the nitromethane solution by distillation and had b. p. 95—100°/0·3 mm. (2·2 g.) (Found: C, 91·2; H, 8·4. Calc. for $C_{15}H_{16}$: C, 91·8; H, 8·2%). Further elution of the column with ether–light petroleum (1 : 9) gave diphenylamine (0·3 g.).

4 : 4′-*Dibromodiazoaminobenzene in bromobenzene.* After pyrolysis of 15 g., *p*-bromoaniline (4·5 g.) was extracted with dilute acid. The crude product obtained on removal of the solvent gave two fractions on distillation: (*a*) a light yellow oil, b. p. 135—140°/0·5 mm. (5·3 g.), and (*b*) 4 : 4′-dibromodiphenyl (1·3 g.). Chromatography of (*a*) on Norite (previously washed with distilled water and dried at 150°) from light petroleum (b. p. 60—80°) afforded 2′ : 4-dibromodiphenyl (2·8 g.). Elution with chloroform–light petroleum (1 : 20) gave 3 : 4′-dibromodiphenyl, b. p. 138—140°/0·5 mm. (0·8 g.) (Found: C, 46·5; H, 2·4. Calc. for $C_{12}H_8Br_2$: C, 46·2; H, 2·6%), and more 4 : 4′-dibromodiphenyl (0·3 g.). Authentic 2′ : 4-dibromodiphenyl was prepared as follows:[13] *p*-bromophenylhydrazine (5 g.) was dissolved in bromobenzene (100 ml.) and silver oxide (10 g.) added gradually with stirring. The mixture was left overnight and then boiled under reflux for 30 min. After cooling, the silver residue was filtered off and the filtrate dried ($MgSO_4$) and distilled. The crude product obtained on removal of the solvent gave a light red oil, b. p. 130—138°/0·3 mm. Chromatography afforded 2′ : 4-dibromodiphenyl as colourless needles, m. p. 55° (0·3 g.), and 4 : 4′-dibromodiphenyl, m. p. 162° (0·6 g.).

4-*Bromodiazoaminobenzene in bromobenzene.* Pyrolysis of 10 g. gave *p*-bromoaniline (2·8 g.) by acid-extraction, and distillation of the residual material yielded an orange oil, b. p. 110—140°/0·5 mm. (5·0 g.); chromatography afforded (*a*) a light yellow oil (4·0 g.) and (*b*) 4-bromodiphenylamine. Further chromatography of (*a*) on Norite with light petroleum (b. p. 60—80°) gave mixed bromodiphenyls, b. p. 105—110°/0·5 mm. (2·8 g.) (Found: Br, 33·9. Calc. for $C_{12}H_9Br$: Br, 34·3%), from which 2-bromo-4′ : 5-dinitrodiphenyl was prepared, as above. Further elution of the column with chloroform–light petroleum (1 : 9) afforded 4-bromodiphenyl (0·3 g.).

4-*Nitrodiazoaminobenzene in bromobenzene.* From 15 g. of the diazoamino-compound, 4 g. of *p*-nitroaniline were obtained and the residue, after removal of the solvent, was distilled, giving (*a*) a light red oil, b. p. 105—125°/0·5 mm. (6·7 g.), and (*b*) a dark red oil, b. p. 155—160°/0·5 mm. (0·6 g.). Chromatography of (*a*) gave mixed bromodiphenyls, b. p. 105—110°/0·5 mm. (5·7 g.) (Found: C, 62·1; H, 4·0. Calc. for $C_{12}H_9Br$: C, 61·8; H, 3·85%), from which 2-bromo-4′ : 5-dinitrodiphenyl was prepared as before. 4-Bromodiphenyl (0·2 g.) was obtained by further elution of the column. Trituration of (*b*) with light petroleum precipitated the insoluble *p*-nitroaniline (0·1 g.) and chromatography of the light petroleum solution on Norite yielded 2-bromo-4′-nitrodiphenyl, m. p. 83° (0·3 g.).

4-*Methoxydiazoaminobenzene in bromobenzene.* Acid-extraction of the solution after pyrolysis of 10 g. gave 3 g. of basic material. Chromatography with ether–light petroleum (3 : 7) gave aniline (1·1 g.) and *p*-anisidine (0·7 g.). The product obtained on removal of the bromo-

[13] Case, *J. Amer. Chem. Soc.*, 1943, **65**, 2137.

benzene was distilled, giving (*a*) an oil, b. p. 125—140°/0·5 mm. (3·8 g.), and (*b*) a fraction, b. p. 145—148°/0·5 mm., which solidified. Crystallised from light petroleum it had m. p. 144° (1·5 g.) and was 4-bromo-4′-methoxydiphenyl. Chromatography of (*a*) gave an oil consisting of a mixture of bromo-4′-methoxydiphenyls and bromodiphenyls, and a solid which crystallised from light petroleum as prisms, m. p. 55° (1·0 g.) (Found: C, 58·6; H, 4·0; Br, 30·3. $C_{13}H_{11}OBr$ requires C, 59·3; H, 4·2; Br, 30·4%). This is 2(or 3)-*bromo-4′-methoxydiphenyl*. The bromodiphenyls and bromomethoxydiphenyls were separated as follows: the crude product (2·3 g.) (after removal of bromobenzene), in glacial acetic acid (25 ml.) and hydrobromic acid (*d* 1·5; 30 ml.), was boiled under reflux for 2 hr. On cooling, the mixture was added to a large excess of sulphurous acid and extracted with ether. The extract was shaken with 5% aqueous sodium hydrogen carbonate and then with 2N-sodium hydroxide. Acidification of the latter and ether-extraction gave a phenolic oil (0·5 g.; equiv. to 0·53 g. of bromo-4′-methoxydiphenyls), which formed a *benzoate*, m. p. 105° (Found: C, 64·5; H, 4·0; Br, 22·3. $C_{19}H_{13}O_2Br$ requires C, 64·6; H, 3·7; Br, 22·7%). Distillation of the ether solution gave mixed bromodiphenyls, b. p. 108—110°/0·6 mm. (1·4 g.) (Found: C, 61·7; H, 4·05. Calc. for $C_{12}H_9Br$: C, 61·8; H, 3·85%). (From a Gomberg reaction with diazotised *p*-anisidine in bromobenzene we isolated 4-bromo-4′-methoxydiphenyl and an oil, b. p. 138—140°/0·5 mm.; the phenol obtained by demethylation of the latter formed a benzoate, m. p. 105°, identical with that described above.)

*4-Bromo-4′-nitrodiazoaminobenzene in bromobenzene.* Pyrolysis of 8 g. followed by acid-extraction gave basic material (2·5 g.). Chromatography with chloroform–light petroleum (7 : 3) gave *p*-nitroaniline (1·9 g.). Distillation of the residue, after removal of the solvent, yielded a light red oil, b. p. 140—162°/0·3 mm. (5·0 g.). Chromatography afforded mixed dibromodiphenyls as a faintly yellow semi-solid (2·5 g.), trituration of which with light petroleum gave 4 : 4′-dibromodiphenyl (0·5 g.). Removal of the light petroleum and distillation gave mixed dibromodiphenyls, b. p. 136—138°/0·5 mm. (1·2 g.) (Found: Br, 51·5. Calc. for $C_{12}H_8Br_2$: Br, 51·2%). Further elution of the column gave 2-bromo-4′-nitrodiphenyl (0·3 g.).

We thank Miss D. A. Thomson for the microanalyses and the University of Aberdeen for a Scholarship (to R. L. H.).

THE UNIVERSITY, OLD ABERDEEN, SCOTLAND. [*Received, November 21st*, 1957.]

---

## 254. *Decomposition Reactions of Heterocyclic Diacyl Peroxides. Part III.*[1] *5-Methyl-1-phenyl-1 : 2 : 3-triazole-4-carbonyl Peroxide.*

By (the late) M. C. FORD and DONALD MACKAY.

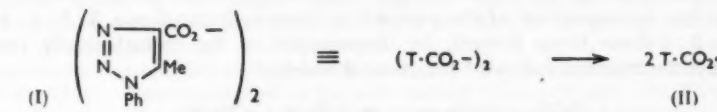
The triazolecarbonyloxy-radicals (II) generated by decomposition of the peroxide (I) resemble 2-thenoyloxy-radicals (Part II) in their behaviour towards aromatic solvents; in particular they attack chlorobenzene and bromobenzene, with displacement of the halogen, to give the phenyl triazolecarboxylate. They dehydrogenate toluene, and, in the presence of oxygen, benzyl hydroperoxide is formed.

THE study of decomposition reactions of representative heterocyclic diacyl peroxides has now been extended to 5-methyl-1-phenyl-1 : 2 : 3-triazole-4-carbonyl peroxide (I), reported by Cooper [2] to be a very active catalyst for vinyl polymerisation.

In aromatic solvents lacking side-chain hydrogen resins were produced, and the chief simple products were the methylphenyltriazole (TH) and the methylphenyltriazolecarboxylic acid (T·$CO_2$H). The formation of the carboxylic acid recalls that of coumarilic acid from coumariloyl peroxide (Part I [3]) and of 2-thenoic acid from 2-thenoyl peroxide [1]

[1] Part II, *J.*, 1957, 4620.
[2] Cooper, *J.*, 1952, 2408.
[3] Ford and Waters, *J.*, 1951, 1824.

in such solvents: it probably arises mainly by processes in which the triazolecarbonyloxy-radicals (II) dehydrogenate solute molecules: the 5-methyl group in the peroxide (and in any species derived from it) would be an obvious point of attack. The methylphenyltriazole, which could have arisen as the result of similar processes involving triazolyl




radicals (T·), was probably, however, an artefact: the triazolecarboxylic acid was independently shown to undergo slow decarboxylation at the temperature of the experiments, and the methylphenyltriazole formed could be accounted for in this way. No other compounds for which reactions of triazolyl radicals could be considered responsible were isolated. The more interesting simple products, obtained in smaller amount, were aryl triazolecarboxylates ($T{\cdot}CO_2Ar$) derived by attack of the triazolecarbonyloxy-radicals on the solvent. They were not formed with the same regularity as were the aryl 2-thenoates from 2-thenoyl peroxide, but the reactions took parallel courses: in particular, the *phenyl* triazoloate was produced in chlorobenzene and bromobenzene, with displacement of the halogen.

In benzene there was no nuclear attack, and in nitrobenzene only traces of the *p*-nitrophenyl triazolecarboxylate were formed. The phenyl ester initially isolated from the decompositions in chlorobenzene and bromobenzene was difficult to purify, and when the latter solvent was used the chief contaminant was shown to be the *p*-bromophenyl triazolecarboxylate. In neither solvent was the fate of the displaced halogen discovered. In the decomposition in bromobenzene, however, the crude carboxylic acid fraction contained a little combined bromine, and the uncrystallisable residues were slightly lachrymatory: if bromination had occurred at the 5-methyl group in the peroxide, or in species derived from it, both 5-bromomethyl-1-phenyl-1 : 2 : 3-triazole-4-carboxylic acid and 5-bromomethyl-1-phenyl-1 : 2 : 3-triazole would be expected as products. The lachrymatory bromomethylphenyltriazole was independently prepared, by the action of *N*-bromosuccinimide in the presence of benzoyl peroxide upon the methylphenyltriazole, but its occurrence in the reaction mixture could not be confirmed.

In toluene, where the decomposition was carried out under nitrogen and under oxygen, there was extensive side-chain attack (equation 1): little resin was formed, and there were increased yields of the methylphenyltriazole and of the triazolecarboxylic acid. Under nitrogen, dibenzyl was formed (cf. Part II). Under oxygen the peroxidic titre of the mixture steadily rose, and the mixture, worked up when the titre had its maximum value, gave benzyl hydroperoxide, and no dibenzyl; some benzyl alcohol (a typical breakdown product of the hydroperoxide) and a small amount of the *o*-tolyl triazolecarboxylate (nuclear attack) were also obtained. In an equimolar mixture of toluene and bromobenzene the toluene reacted preferentially: dibenzyl was formed, and no product derived from the bromobenzene was isolated.

$$T{\cdot}CO_2{\cdot} + Ph{\cdot}CH_3 \longrightarrow T{\cdot}CO_2H + Ph{\cdot}CH_2{\cdot} \quad . . . . . (1)$$
$$Ph{\cdot}CH_2{\cdot} + O_2 \longrightarrow Ph{\cdot}CH_2{\cdot}O_2{\cdot} \quad . . . . . (2)$$
$$Ph{\cdot}CH_2{\cdot}O_2{\cdot} + Ph{\cdot}CH_3 \longrightarrow Ph{\cdot}CH_2{\cdot}O_2H + Ph{\cdot}CH_2{\cdot} \quad . . . . . (3)$$

Walling and Buckler [4] prepared benzyl hydroperoxide, by the action of oxygen on ethereal benzylmagnesium chloride, but did not characterise it. Like these authors we were unable to obtain the hydroperoxide analytically pure, but we have made a crystalline

[4] Walling and Buckler, *J. Amer. Chem. Soc.*, 1955, **77**, 6032.

derivative, benzyl triphenylmethyl peroxide. Toluene does not readily undergo autoxidation,[5] and in the present work the yields of hydroperoxide were found to be roughly proportional to the amount of the triazolecarbonyl peroxide used, showing that the sequence (2–3) was self-sustaining only to a negligible extent.

The dehydrogenating properties of the triazolecarbonyloxy-radicals were further exhibited in the decomposition of the peroxide in 3-methylbutan-2-one, 3 : 3 : 4 : 4-tetramethylhexa-2 : 5-dione being formed, by dimerisation of the metathetically produced 1 : 1-dimethyl-2-oxopropyl radicals [6] (reactions 4 and 5).

$$T{\cdot}CO_2{\cdot} + CHMe_2Ac \longrightarrow T{\cdot}CO_2H + {\cdot}CMe2Ac \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$2{\cdot}CMe_2Ac \longrightarrow (CMe_2Ac)_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

## Experimental

The aromatic solvents were purified as described in Part II. Commercial 3-methylbutan-2-one was shaken repeatedly with small portions of saturated aqueous ferrous sulphate, dried ($MgSO_4$), and fractionated, then having b. p. 93°/755 mm.

*5-Methyl-1-phenyl-1 : 2 : 3-triazole-4-carbonyl Peroxide.*—Treatment of 5-methyl-1-phenyl-1 : 2 : 3-triazole-4-carboxylic acid [7] with a large excess of thionyl chloride gave the triazolecarbonyl chloride, which was obtained directly pure (m. p. 133°). A solution of the acid chloride (10 g.) in methylene chloride (50 ml.) was added dropwise to a vigorously stirred ice-cold mixture of 2N-sodium hydroxide and aqueous hydrogen peroxide (30-vol.; 40 ml.). Water then was added and stirring continued for a further 15 min. The methylene chloride was removed by bubbling air through the mixture, the solid being then collected, air-dried, and dissolved in methylene chloride (0·5 l.). Gradual addition, with stirring, of light petroleum (b. p. 30—40°; 1 l.) to the dried ($MgSO_4$) solution gave the peroxide (70%) as crystals, m. p. 167° (sharp, with subsequent decomp.) [Found: equiv. (iodometric) 196. Calc. for $C_{26}H_{16}O_4N_6$: equiv., 202). Cooper [8] records m. p. 166° (decomp.).

*Decomposition Reactions.*—The reaction mixtures were worked up as described in Part II. In all cases recrystallisation of the carboxylic acid fraction from water gave pure methylphenyltriazolecarboxylic acid.

*Benzene.* A solution of the peroxide (5·3 g.) in benzene (1·5 l.) was refluxed under nitrogen. After 48 hr., when 94% of the peroxide had decomposed, 1·0 mole of carbon dioxide (per mole of peroxide) had been evolved. The residual peroxide was destroyed (sodium iodide in acetic acid followed by aqueous sodium sulphite); the benzene layer then gave the triazolecarboxylic acid (2·6 g.) and non-acidic material, which was distilled: the resulting oil, b. p. 165°/0·4 mm., solidified, and was obtained as prisms (0·8 g.), m. p. 64°, from ether–light petroleum (b. p. 50—60°) (Found: C, 67·9; H, 5·7; N, 26·6. Calc. for $C_9H_9N_3$: C, 67·9; H, 5·7; N, 26·4%), identical with authentic 5-methyl-1-phenyl-1 : 2 : 3-triazole, m. p. 64°, prepared [7] by heating the triazolecarboxylic acid above its m. p.

*Nitrobenzene.* Decomposition of the peroxide (6·0 g.) in nitrobenzene (600 ml.) for 8 hr. at 99—106° gave the triazolecarboxylic acid and a tarry residue, which on extraction with hot alcohol yielded a solid (100 mg.): recrystallisation (alcohol) gave *p-nitrophenyl 5-methyl-1-phenyl-1 : 2 : 3-triazole-4-carboxylate* as colourless needles, m. p. 224° (Found: C, 59·1; H, 3·8. $C_{16}H_{12}O_4N_4$ requires C, 59·3; H, 3·7; N, 17·3%). The m. p. was undepressed in admixture with an authentic specimen, m. p. 224° (Found: C, 59·5; H, 3·5; N, 17·1%), prepared by refluxing the triazolecarbonyl chloride with *p*-nitrophenol in pyridine.

*Chlorobenzene.* Decomposition of the peroxide (6·0 g.) in chlorobenzene (600 ml.) at 85—90° for 8 hr. gave the triazolecarboxylic acid (2·3 g.) and a gum (3·6 g.), which on trituration with methanol yielded a solid (0·66 g.) containing traces of combined chlorine: repeated recrystallisation from light petroleum (b. p. 80—90°) afforded *phenyl 5-methyl-1-phenyl-1 : 2 : 3-triazole-4-carboxylate* (0·38 g.) as prisms, m. p. and mixed m. p. 146° (Found: C, 68·6; H, 4·7; N, 15·0. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7; N, 15·0%). Hydrolysis with 2N-sodium

[5] B.P. 707,006; Hock and Lang, *Ber.*, 1943, **76**, 169; Seergeev and Fedorova, *Doklady Akad. Nauk S.S.S.R.*, 1956, **109**, 796.
[6] Kharasch, McBay, and Urry, *J. Amer. Chem. Soc.*, 1948, **70**, 1269.
[7] Dimroth, *Ber.*, 1902, **35**, 1029.

hydroxide yielded the triazolecarboxylic acid, m. p. and mixed m. p. 148—149°, together with phenol (3 : 5-dinitrobenzoate, m. p. and mixed m. p. 145·5°). The authentic ester, m. p. 146° (Found: C, 68·9; H, 4·75; N, 15·0%), was prepared from the acid chloride and phenol in pyridine.

The methanol-soluble fraction was chromatographed on alumina from benzene solution, and yielded traces of the phenyl ester, together with an oil, which when further chromatographed, from ether–light petroleum (b. p. 40—60°) (2 : 1), gave a small quantity of the methylphenyltriazole.

*Bromobenzene.* A solution of the peroxide (7·5 g.) in bromobenzene (750 ml.) was heated at 80—85° for 36 hr. Recrystallisation of the acid fraction (3·2 g.) (Found: Br, 3·1%) gave the triazolecarboxylic acid. The non-acidic material (4·8 g.) was extracted with hot benzene, and the extract was passed down a short alumina column. Removal of the benzene and trituration of the resulting gum with ether–light petroleum (b. p. 30—40°) gave an ester fraction (0·52 g.) (Found: Br, 9·6%), which was chromatographed on Norit from chloroform–light petroleum (b. p. 60—70°) (1 : 8): elution, with this mixture containing an increasing proportion of chloroform, first gave some crystalline material of indefinite m. p., and then the phenyl ester, m. p. and mixed m. p. 144—144·5° (from methanol). Chromatography of the ether–petroleum-soluble material gave the methylphenyltriazole (0·47 g.).

In another experiment the ester fraction was hydrolysed with aqueous-methanolic sodium hydroxide, and gave the triazolecarboxylic acid and a phenolic fraction, which was benzoylated: recrystallisation of the product from light petroleum (b. p. 30—40°) gave prisms, m. p. 99—102°, undepressed in admixture with *p*-bromophenyl benzoate.

*Toluene.* (*a*) Under nitrogen. When a suspension of the peroxide (5·2 g.) in toluene (580 ml.) was heated under nitrogen at 90—95° for 3 days the triazolecarboxylic acid (1·7 g.) and a non-acidic fraction (4·7 g.) were obtained: chromatography of the latter on alumina from ether–light petroleum (b. p. 30—40°) solution yielded dibenzyl (0·82 g.), m. p. and mixed m. p. 50—51°, and the methylphenyltriazole (2·1 g.).

(*b*) Under oxygen. Dry oxygen was slowly bubbled through a suspension of the peroxide (3·0 g.) in toluene (305 ml.) at 75—85°: the iodometric titre of the mixture reached its maximum after 4½ days, having then increased by 140%. After removal of the triazolecarboxylic acid (1·0 g.) the almost colourless solution was extracted with 2N-sodium hydroxide: acidification of the extracts gave an oil (1·5 g.), which was isolated with ether. Further quantities of the peroxide (12 g. in all) were similarly decomposed, and the alkali-soluble oil, benzyl hydroperoxide (see below), was accumulated.

The non-acidic fractions from these decompositions were combined (7·2 g.) and triturated with ether–light petroleum (b. p. 30—40°): the resulting solid (0·95 g.) was recrystallised (twice) from benzene–light petroleum (b. p. 80—90°) and finally from methanol, giving *o-tolyl 5-methyl-1-phenyl-1 : 2 : 3-triazole-4-carboxylate* as prisms, m. p. 138—139° (Found: C, 69·7; H, 5·0. $C_{17}H_{15}O_2N_3$ requires C, 69·6; H, 5·1; N, 14·3%), identical with a specimen, m. p. 142° (Found: C, 69·4; H, 5·1; N, 14·3%), prepared from the acid chloride and *o*-cresol in pyridine.

Fractionation of the mother-liquor from the initial separation of the ester gave benzyl alcohol (1·9 g.) (1-naphthylcarbamate, m. p. and mixed m. p. 130—131°) and the methylphenyltriazole (2·0 g.). No dibenzyl was isolated.

*Toluene–bromobenzene.* A suspension of the peroxide (6·0 g.) in a mixture of toluene (305 ml.) and bromobenzene (300 ml.) heated at 85—95° for 38 hr. under nitrogen gave the triazolecarboxylic acid (1·7 g.) and an oil, which was chromatographed on alumina, first from benzene–light petroleum (b. p. 80—90°) (1 : 1) and then from light petroleum (b. p. 50—60°): dibenzyl (0·7 g.) and the methylphenyltriazole (0·9 g.) were obtained.

*3-Methylbutan-2-one.* A suspension of the peroxide (5·4 g.) in the ketone (270 ml.) was refluxed for 8 hr. under nitrogen. The mixture gave the triazolecarboxylic acid (3·4 g.) and an oil, which afforded 3 : 3 : 4 : 4-tetramethylhexa-2 : 5-dione (0·5 g.), b. p. 70—80°/1·0 mm., identified by conversion into its tetrabromo-derivative, obtained as rods, m. p. 117·5°, from methanol (lit.,[6] 117°) (Found: Br, 65·8. Calc. for $C_{10}H_{14}O_2Br_4$: Br, 65·8%), and a higher-boiling fraction (1·0 g.) consisting substantially of the methylphenyltriazole.

*Decarboxylation of 5-Methyl-1-phenyl-1 : 2 : 3-triazole-4-carboxylic acid in Boiling Benzene.*—The concentration of a *ca.* 0·01N-solution of the acid in benzene was determined by shaking an aliquot part with an excess of 0·05N-sodium hydroxide and back-titrating it with 0·01N-hydrochloric acid. The solution was refluxed for 3 days and the determination repeated: the figures

obtained showed that 45% of the acid had undergone decarboxylation. The methylphenyltriazole was isolated from the solution.

*Bromination of 5-Methyl-1-phenyl-1 : 2 : 3-triazole.*—A solution of the triazole (2·6 g.) in carbon tetrachloride (30 ml.) was refluxed with *N*-bromosuccinimide (4·0 g.) for 12 hr., a crystal of benzoyl peroxide being introduced at intervals during the first hour. The mixture was filtered and the filtrate taken to dryness: repeated extraction of the residue with hot ether–light petroleum (b. p. 50—60°) and evaporation of the extracts yielded crystals (0·5 g.) which on recrystallisation from light petroleum gave the slightly lachrymatory *5-bromomethyl-1-phenyl-1 : 2 : 3-triazole* as prisms, m. p. 66° (Found: C, 45·7; H, 3·3; N, 17·9; Br, 33·0. $C_9H_8N_3Br$ requires C, 45·4; H, 3·4; N, 17·7; Br, 33·6%). Proof of side-chain bromination was obtained by oxidation to 1-phenyl-1 : 2 : 3-triazole-5-carboxylic acid, m. p. 172—174°, identical with an authentic specimen.[7]

*Characterisation of Benzyl Hydroperoxide.*—When a small quantity of the alkali-soluble oil obtained from the reactions in toluene under oxygen was heated at atmospheric pressure, decomposition set in with vigour, yielding benzaldehyde (2 : 4-dinitrophenylhydrazone, m. p. 238°), benzyl alcohol (1-naphthylcarbamate, m. p. 131°), and water. Attempted distillation at 0·01 mm. from glass wool (bath $>$50°) resulted in an explosion, but distillation under nitrogen gave the hydroperoxide as a colourless liquid, b. p. 50—51°/0·01 mm. (lit.,[4] 55—57°/0·1 mm.) [Found: equiv. (iodometric), 55. Calc. for $C_7H_8O_2$: equiv., 62], with a faint "metallic" odour and skin-irritant properties. Treatment of a glacial acetic acid solution with triphenylmethanol and a trace of concentrated sulphuric acid [8] gave *benzyl triphenylmethyl peroxide*, which formed large prisms, m. p. 82°, from light petroleum (b. p. 60—70°) [Found (combustion in air): C, 85·2; H, 6·0. $C_{26}H_{22}O_2$ requires C, 85·2; H, 6·05%] and appeared to be stable indefinitely.

A reference sample of the hydroperoxide was obtained, in low yield, by portion-wise addition of ethereal benzylmagnesium chloride, with stirring, to oxygen-saturated ether (cooled by solid carbon dioxide–methanol) at such a rate that the internal temperature remained between −50° and −60°; dropwise addition [4] of the Grignard solution led to a very much poorer yield. The triphenylmethyl derivative, m. p. 82° (Found: C, 85·3; H, 6·0%), was identical with the above.

One of us (D. M.) thanks the Carnegie Trust for the Universities of Scotland for a scholarship and the Murdo Macaulay Trust for a grant. Microanalyses are by Miss D. A. Thomson.

THE UNIVERSITY, OLD ABERDEEN. [*Received, August 9th*, 1957.]

[8] Davies, Foster, and White, *J.*, 1954, 2200.

---

## 255. *Decomposition Reactions of Heterocyclic Diacyl Peroxides. Part IV.*[1] *Nicotinoyl Peroxide.*

By (the late) M. C. FORD and DONALD MACKAY.

Decomposition of nicotinoyl peroxide generates 3-pyridyl radicals, which attack aromatic solvents to give 3-arylpyridines.

IT was expected that nicotinoyl peroxide would provide a contrast with the peroxides previously examined, and would resemble an aroyl peroxide in its decompositions.

The great ease with which nicotinoyl chloride is hydrolysed makes the preparation of the peroxide difficult: Milas and Panagiotakos [2] obtained it, in low yield, by addition of the ethereal acid chloride to aqueous sodium peroxide; a more easily purified product was obtained by treatment of an ethereal mixture of the acid chloride and pyridine, at −70°, with ethereal hydrogen peroxide.

[4] Yields are calculated on the equation: $(R{\cdot}CO_2)_2 + ArH \longrightarrow ArR + CO_2 + R{\cdot}CO_2H$.

[1] Part II, *J.*, 1957, 4620; Part III, preceding paper.
[2] Milas and Panagiotakos, *J. Amer. Chem. Soc.*, 1940, **62**, 1878.

Decomposition of the peroxide in aromatic solvents gave 3-arylpyridines: 3-phenylpyridine (55% *) was formed in benzene, 3-tolylpyridines (36%) in toluene, 3-nitrophenylpyridines (70%) in nitrobenzene, and 3-bromophenylpyridines, in low yield, in bromobenzene. The mixture of nitrophenylpyridines consisted chiefly of the 3-*o*-isomer, along with smaller amounts of the 3-*p*-isomer: both were obtained pure. Oxidative degradation showed that the tolylpyridine mixture likewise contained 3-*o*- and 3-*p*-isomers. The 3-*m*-isomers were almost certainly produced, but in neither case was their presence in the mixture definitely established.

Aryl nicotinates were probably also formed, though in very small amount (cf. Parts II and III), for the crude arylpyridine fractions gave only traces of phenolic material when boiled with acid or alkali. In solvents lacking side-chain hydrogen traces of pyridine were produced, but in toluene a larger amount was formed, and, in addition to the tolylpyridines, dibenzyl was isolated. The proportion of side-chain attack (for which 3-pyridyl radicals were evidently responsible) appeared to be rather high: the mixture of dibenzyl and diaryls obtained by decomposition of benzoyl peroxide in toluene contains 13% by weight of dibenzyl,[3] corresponding to a molar ratio (dibenzyl : diaryls) of 0·14; with nicotinoyl peroxide the molar ratio was *ca.* 0·2.

## Experimental

*Nicotinoyl Peroxide.*—Moisture was rigidly excluded throughout. Dropwise addition of thionyl chloride (108 ml., 3 mol.) to dry sodium nicotinate (73 g.) at room temperature caused an exothermic reaction. The mixture was heated under reflux for 1 hr. at 100°, the excess of thionyl chloride was removed, and the nicotinoyl chloride (64 g., 90%) slowly distilled at *ca.* 10 mm. (free flame) from the sodium chloride. Redistillation under dry nitrogen gave a colourless liquid, b. p. 90°/13 mm. (lit.,[4] 85°/12 mm.).

Pyridine (2·9 ml., 1 mol.) was added to the acid chloride (5 g.) in dry ether (50 ml.); the mixture was set aside for 5 min. and then cooled to −70°: freshly prepared 1·5N-ethereal hydrogen peroxide (dried over $CaSO_4$; 50 ml.) was added dropwise, with stirring, and the mixture then allowed to warm to room temperature and filtered. The filtrate was washed sparingly with 2N-potassium hydrogen carbonate and water, and dried ($MgSO_4$), the ether was removed, and the residue (1·5 g.) washed with light petroleum (b. p. 30—40°). Several preparations were carried out and the product was accumulated and stirred with cold benzene : nicotinic acid was filtered off. Addition of light petroleum to the filtrate first precipitated traces of the acid, and then the peroxide (15—20%), prisms, m. p. 92° (lit.,[2] 88—89°) [Found: equiv. (iodometric in 2N-sulphuric acid), 118. Calc. for $C_{12}H_8O_4N_2$: equiv., 122]; the purity (97%) was increased to 99% by a further recrystallisation (lit.,[2] purity 93—98·5%).

*Decomposition in Aromatic Solvents.*—The reaction mixtures were worked up as follows. The solvent was removed, through a column, at a suitable pressure (cold-trap) and the appropriate cut was combined with the trap-condensate and the whole extracted with 2N-sulphuric acid; the extract was basified and distilled: pyridine in the distillate was characterised as the picrate and determined as dipyridinecopper(II) thiocyanate. Nicotinic acid crystallised from the concentrate, and was completely removed by treatment of the mother-liquor with ether–light petroleum; recrystallisation gave the pure acid. The residual non-acidic material was treated as described.

*Benzene.* A solution of the peroxide (8·13 g.) in benzene (813 ml.) was refluxed for 48 hr.: carbon dioxide (1·3 moles per mole of peroxide), pyridine (100 mg.), nicotinic acid (1·4 g.), and an oil (3·74 g.), b. p. <70°/0·01 mm., which was substantially 3-phenylpyridine, were produced. A portion of the oil (0·65 g.) was refluxed with 2N-sodium hydroxide, giving phenol (9 mg.) (*s*-tribromophenol, m. p. 91·5°), recovered (0·63 g.), and treated with a slight excess of methanolic picric acid: recrystallisation of the precipitate from acetone–methanol gave 3-phenylpyridine picrate (1·2 g.), m. p. and mixed m. p. 159—160° (Found: C, 53·2; H, 3·3; N, 14·4. Calc. for $C_{17}H_{12}O_7N_4$: C, 53·1; H, 3·1; N, 14·6%), from which pure 3-phenylpyridine was liberated as a colourless oil, b. p. 98—102°/0·7 mm. The *picrolonate* formed orange-yellow plates, m. p. 208°

[3] Hey, Pengilly, and Williams, *J.*, 1956, 1461.
[4] Meyer and Graf, *Ber.*, 1928, **61**, 2205.

XUM

(decomp.), from acetone–methanol (Found: C, 59·9; H, 4·1; N, 16·4. $C_{21}H_{17}O_5N_5$ requires C, 60·1; H, 4·1; N, 16·7%).

*Nitrobenzene.* Decomposition of the peroxide (5·2 g.) in nitrobenzene (520 ml.) at 85—90° for 24 hr. gave carbon dioxide (0·62 mol.), pyridine (20 mg.), nicotinic acid (2·6 g.) and non-acidic material which on trituration with ether furnished 3-*p*-nitrophenylpyridine, obtained as cream-coloured needles (0·47 g.), m. p. 148° (lit.,[5] 148—149°), after recrystallisation (twice) from methanol (Found: C, 66·0; H, 4·2; N, 13·8. Calc. for $C_{11}H_8O_2N_2$: C, 66·0; H, 4·0; N, 14·0%); the picrate crystallised from acetone–methanol as yellow prisms, m. p. 218—219° (decomp.) (lit.,[6] 220°) (Found: N, 16·2. Calc. for $C_{17}H_{11}O_9N_5$: N, 16·3%). The ethereal mother-liquor was evaporated and distilled: removal of traces of the 3-*p*-isomer from the distillate (b. p. 120—140°/0·01 mm.) gave a pale yellow oil (A) (2·5 g.).

Chromatography of the oil A (0·46 g.) on basic alumina from ether–light petroleum (1 : 2) solution gave mainly oily 3-*o*-nitrophenylpyridine (Found: C, 66·0; H, 4·1%); the picrate formed yellow needles, m. p. 182—183° (lit.,[6] 182—183°), after a single recrystallisation from acetone–methanol (Found: N, 16·0%). The oil A (1·6 g.) was recovered almost quantitatively after 2 hr. in refluxing 30% sulphuric acid, only traces of nitrophenols being produced. Quaternisation of the recovered material with methyl sulphate followed by treatment of the product in turn with 2N-sodium hydroxide and boiling aqueous permanganate yielded a mixture of nitrobenzoic acids (0·18 g.): fractional crystallisation from water gave the pure *o*-isomer, m. p. and mixed m. p. 144—145°, after recrystallisation from toluene; no *m*-isomer could be isolated.

*Toluene.* Decomposition of the peroxide (6·93 g.) in toluene (710 ml.) under nitrogen at 70—75° for 70 hr. gave carbon dioxide (1·0 mol.), pyridine (1·0 g.), nicotinic acid (2·3 g.), and non-acidic material. The latter was separated into a neutral fraction, which was chromatographed on alumina from light petroleum (b. p. 30—40°) solution, giving dibenzyl (0·42 g., 2·3 mmoles), m. p. and mixed m. p. 51—52° (methanol), and a basic fraction (2·3 g.), which was refluxed with 5N-sodium hydroxide (giving 17 mg. of phenolic material), recovered (2·1 g.), and heated with a slight excess of methanolic picric acid: a mixture of 3-tolylpyridine picrates (4·1 g., 10·3 mmoles), m. p. 152—156° (Found: C, 54·1; H, 3·7; N, 13·8. Calc. for $C_{18}H_{14}O_7N_4$: C, 54·3; H, 3·5; N, 14·1%), resulted, from which the mixed 3-tolylpyridines (1·5 g.), b. p. 100—110°/1·0 mm., were liberated. A portion gave a mixture of picrolonates, m. p. 163—165° (decomp.) (Found: N, 16·0. Calc. for $C_{22}H_{19}O_5N_5$: N, 16·2%), which, like that of the picrates, was not amenable to fractional crystallisation. Another portion, on quaternisation (methyl iodide) and oxidation, gave phthalic acid (anhydride, m. p. 128°) and terephthalic acid, subl. >300°; no *iso*phthalic acid could be isolated.

*Bromobenzene.* Decomposition of the peroxide (2·2 g.) in bromobenzene (220 ml.) at 80—85° for 20 hr. gave a trace of pyridine, nicotinic acid, and an oil, which was refluxed with 30% sulphuric acid (giving 12 mg. of phenolic material), recovered, and treated with methanolic picric acid: a mixture of 3-bromophenylpyridine picrates (0·16 g.), m. p. 174—180°, resulted (Found: C, 43·8; H, 2·6; Br, 17·4. Calc. for $C_{17}H_{11}O_7N_4Br$: C, 44·0; H, 2·4; Br, 17·3%).

An authentic specimen of 3-phenylpyridine picrate was kindly supplied by Professor D. H. Hey, F.R.S. One of us (D. M.) thanks the Carnegie Trust for the Universities of Scotland for a scholarship and the Murdo Macaulay Trust for a grant. Microanalyses are by Miss D. A. Thomson.

THE UNIVERSITY, OLD ABERDEEN. [*Received, August 9th,* 1957.]

[5] Forsyth and Pyman, *J.*, 1926, 2912.
[6] Haworth, Heilbron, and Hey, *J.*, 1940, 349.

XUM

## 256. *Some Unsymmetrical Azo-nitriles.*

By (the late) M. C. Ford and R. A. Rust.

Oxidation with bromine of hydrazo-nitriles R·NH·NH·$CMe_2$·CN (R = Ar or $CO_2Me$), obtained by adaption of standard methods,[1,2] gave the corresponding azo-nitriles, R·N:N·$CMe_2$·CN, in good yield. It was thought that these would decompose at moderate temperatures to yield 1-cyano-1-methylethyl (2-cyano-2-propyl) radicals together with aryl or methoxycarbonyl radicals:

$$R\cdot N{:}N\cdot CMe_2\cdot CN \longrightarrow R\cdot + N_2 + \cdot CMe_2\cdot CN$$

However, they proved too stable for an investigation of their decomposition in organic solvents to be profitable.

When α-(phenylazo)*iso*butyronitrile, Ph·N:N·$CMe_2$·CN, was heated in the presence of iodine small quantities of iodobenzene and α-iodo*iso*butyronitrile were formed, indicating that homolysis of the azo-nitrile occurred to some extent. Pyrolysis of the azo-nitrile gave very low yields of simple products: these were tetramethylsuccinonitrile (the typical dimer of 2-cyano-2-propyl radicals [3]), benzene, α-methylacrylonitrile, and an oil which was probably a mixture of α- and β-phenyl*iso*butyronitrile.

Pyrolysis of α-(methoxycarbonylazo)*iso*butyronitrile, $MeO_2C$·N:N·$CMe_2$·CN, gave methyl α-cyano*iso*butyrate, in small yield. No tetramethylsuccinonitrile was isolated, and, in the presence of iodine, no iodo-nitrile was formed, suggesting that the decomposition probably occurred by an intramolecular process not involving free radicals.

*Experimental.—Hydrazino-nitriles.* A mixture of phenylhydrazine (50 ml., 0·5 mole), acetone cyanohydrin (45 ml., 0·5 mole), and ether (13 ml.) was set aside in a pressure-bottle at room temperature for 8 days: α-phenylhydrazino*iso*butyronitrile gradually crystallised; air-dried and recrystallised from ether–light petroleum (b. p. 80—90°) it gave prisms (66 g., 75%), m. p. 69° (lit.,[2] 70°) (Found: C, 68·9; H, 7·5; N, 23·7. Calc. for $C_{10}H_{13}N_3$: C, 68·5; H, 7·5; N, 24·0%).

α-m-*Tolyl*-, prisms, m. p. 86·5—87° (Found: C, 69·9; H, 8·1; N, 22·3. $C_{11}H_{15}N_3$ requires C, 69·8; H, 8·0; N, 22·2%), and α-p-*tolyl-hydrazinoisobutyronitrile*, needles, m. p. 94·5—96·5° (Found: C, 69·7; H, 8·0; N, 22·0%) (both from ether–light petroleum), were prepared similarly, 100% excess of the cyanohydrin being used in the preparation of the latter.

Methyl hydrazinoformate [4] (18 g., 0·2 mole) and acetone cyanohydrin (45 ml.) were heated together in a pressure-bottle at 100° for 7½ hr. Concentration under reduced pressure and recrystallisation of the residue from benzene–light petroleum gave α-N′-*methoxycarbonylhydrazinoisobutyronitrile* (20 g., 65%) as needles, m. p. 99—101° (Found: C, 46·0; H, 7·2; N, 26·9. $C_6H_{11}O_2N_3$ requires C, 45·8; H, 7·05; N, 26·7%).

*Azo-nitriles.* A saturated solution of bromine in 15% aqueous potassium bromide was added in portions, with shaking, to one of phenyl hydrazino-nitrile (50 g.) in chloroform (140 ml.), the temperature being maintained at *ca.* 0° by addition of ice. When the aqueous layer was permanently yellow the chloroform layer was separated, shaken in turn with aqueous sodium sulphite, 2N-sodium carbonate, and water, and dried ($MgSO_4$). Removal of the solvent left an orange liquid, which yielded α-(*phenylazo*)*isobutyronitrile* (40 g., 82%) as a yellow oil, b. p. 64°/0·05 mm., $d_D^{19}$ 1·011, $n_D^{19}$ 1·5284, with a penetrating odour (Found: C, 69·6; H, 6·6; N, 24·4. $C_{10}H_{11}N_3$ requires C, 69·3; H, 6·4; N, 24·3%). The light absorption, $\lambda_{max.}$ 270 mμ and 390 mμ (log ε 3·81 and 2·30 respectively), resembled that of phenylazomethane.[5] A solution in concentrated sulphuric acid, set aside for 12 hr. and then poured on ice, gave α-(*phenylazo*)*isobutyramide*, yellow needles, m. p. 65·5—67°, from light petroleum (b. p. 40—60°) (Found: C, 62·8; H, 7·0; N, 22·3. $C_{10}H_{13}ON_3$ requires C, 62·8; H, 6·85; N, 22·0%).

[1] Reissert, *Ber.*, 1884, **17**, 1458.
[2] Bucherer and Grolée, *Ber.*, 1906, **39**, 1005.
[3] Bickel and Waters, *Rec. Trav. chim.*, 1950, **69**, 1490.
[4] Diels, *Ber.*, 1914, **47**, 2187.
[5] Burawoy, *J.*, 1937, 1865.

XUM

Pyrolysis of the azo-nitrile (50 g.) at *ca.* 180°, in five portions, gave benzene (1·7 g.) (*m*-dinitrobenzene, m. p. 89°), a little α-methylacrylonitrile, tetramethylsuccinonitrile (1·2 g.), m. p. and mixed m. p. 166—168°, and an oil (3 g.), b. p. 90—96°/10 mm. (Found: C, 82·2; H, 7·7; N, 9·8%), probably a mixture of α- and β-phenyl*iso*butyronitrile (Calc. for $C_{10}H_{11}N$: C, 82·7; H, 7·6; N, 9·6%), which could not be separated by means of solid derivatives. Much intractable material of higher molecular weight was also formed.

Gradual addition of the azo-nitrile (4·3 g.) to iodine (6·3 g.) in boiling toluene (10 ml.), followed by 2 hours' refluxing, gave α-iodo*iso*butyronitrile (0·3 g.) (α-iodo*iso*butyramide,[6] m. p. 181—182°) and iodobenzene (0·3 g.) (*p*-iodonitrobenzene, m. p. 169—170°).

α-(m-*Tolylazo*)iso*butyronitrile*, an orange-yellow oil, b. p. 68·5°/0·04 mm., $n_D^{25}$ 1·5245 (Found: C, 70·3; H, 6·9; N, 22·4. $C_{11}H_{13}N_3$ requires C, 70·6; H, 7·0; N, 22·4%) [α-(m-*tolylazo*)iso*butyramide*, yellow needles, m. p. 82·5—83·5° (Found: C, 64·6; H, 7·3; N, 20·2. $C_{11}H_{15}ON_3$ requires C, 64·4; H, 7·4; N, 20·5%)], and α-(p-*tolylazo*)iso*butyronitrile*, pale yellow needles, m. p. 55·5—58° (Found: C, 70·4; H, 6·9; N, 22·2%), were prepared similarly.

α-(*Methoxycarbonylazo*)iso*butyronitrile*. The hydrazino-compound (10 g.) in chloroform (50 ml.) was oxidised as above. The purified chloroform extracts from five such oxidations were combined, and yielded the *azo-compound* (31 g., 65%) as a pleasant-smelling lemon-yellow oil, b. p. 54°/0·01 mm., $d_D^{19}$ 1·064, $n_D^{25}$ 1·4266 (Found: C, 46·7; H, 5·7; N, 26·8. $C_6H_9O_2N_3$ requires C, 46·4; H, 5·85; N, 27·1%). Oxidation in larger batches led to poor yields. Cautious pyrolysis of the azo-compound (23 g.) at *ca.* 170°, in ten portions, gave methyl α-cyano*iso*butyrate (2·5 g.), b. p. 70—72°/17 mm. (lit.,[7] 76—78°/20 mm.), characterised by conversion[7] into dimethylmalonic acid, m. p. and mixed m. p. 189—191°.

One of us (R. A. R.) thanks the University of Aberdeen for a scholarship and the D.S.I.R. for a maintenance grant.

THE UNIVERSITY, OLD ABERDEEN. [*Received, August 9th*, 1957.]

[6] Ford and Waters, *J.*, 1951, 1851.
[7] Hesse, *Amer. Chem. J.*, 1896, **18**, 743.

---

## 257. *The Effect of Urea on the Streaming Birefringence and Viscosity of Sodium Deoxyribonucleate.*

By A. R. MATHIESON and M. R. PORTER.

THE effect of urea on aqueous solutions of sodium deoxyribonucleate (DNA) was studied by Butler and Conway [1] who found that, after removal of the urea by dialysis, there is a reduction in the viscosity and the extent of hysteresis in the titration curves, together with an increase in the sedimentation and diffusion constants. They ascribed these changes to the effect on the DNA molecule of the breaking of hydrogen bonds by the urea.

We have studied the effect of urea at 25° in presence of 0·2M-sodium chloride on the viscosity and streaming birefringence of DNA. The sample of DNA employed was extracted from calf-thymus glands and has been fully described elsewhere.[2] Measurements were made on solutions of DNA in 0·2M-sodium chloride solution after the urea had been removed by dialysis. The effects of the time of contact with urea, and of the urea concentration are shown in Fig. 1 for solutions of DNA for which $\chi°$ (orientation angle) is independent of DNA concentration. A 1·0M-urea solution has no detectable effect during 22 hours, but a 5·0M-urea solution has a small but significant influence on $\chi$ during 2—48 hours. The values of the rotary-diffusion constant ($\theta$), calculated from these results by considering the DNA molecule to be a prolate ellipsoid of revolution, and by using Peterlin

[1] Butler and Conway, *J.*, 1952, 3075.
[2] Jordan, Mathieson, and Matty, *J.*, 1956, 154.

and Stuart's [3] equations, are $\theta = 10$ sec.$^{-1}$ for untreated solutions and for solutions treated with 1M-urea, and $\theta = 16$ sec.$^{-1}$ for solutions treated with 5M-urea. A 0·022% solution of DNA in 5M-urea and 0·2M-sodium chloride has pH 8·4. No alkaline denaturation should have occurred under these conditions [4] but as a check the value of $\theta$ was measured for DNA in 0·2M-sodium chloride at pH 8·9; $\theta = 9{\cdot}0$ sec.$^{-1}$ was found. The intrinsic viscosity at zero shear ($[\eta]$) was measured for DNA in 0·2M-sodium chloride solution. For DNA which

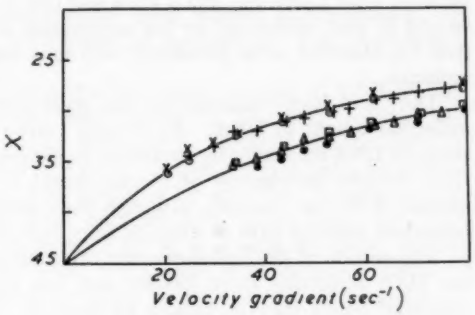



FIG. 1. *Effect of urea on the birefringence of nucleic acid in presence of* 0·2M-*sodium chloride* (*nucleic acid concn.*: 0·026%).

× *Untreated.*
○ 1M-*Urea for* 75 *min.*
\+ 1M-*Urea for* 22 *hr.*
● 5M-*Urea for* 105 min.
△ 5M-*Urea for* 20 *hr.*
⊡ 5M-*Urea for* 48 *hr.*

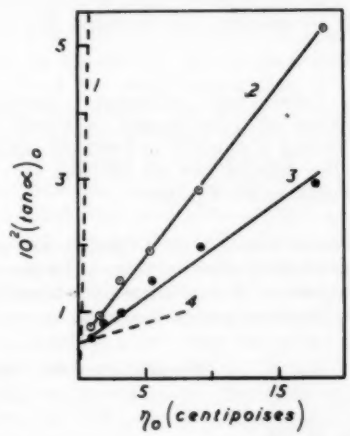



FIG. 2. *Effect of solvent viscosity on* $(\tan \alpha)_0$.

1, *Tobacco-mosaic virus.*
2, *Nucleic acid.*
3, *Nucleic acid in presence of* 5M-*urea.*
4, *Polystyrene.*

had been treated with a 5M-urea solution $[\eta] = 40{\cdot}7$ ($c$ in %) and for untreated DNA $[\eta] = 52{\cdot}5$.

The increase in $\theta$ and decrease in $[\eta]$ brought about by 5M-solutions indicate either that the DNA molecules have been degraded or that they have lost some of their rigidity with a decrease in their extreme assymmetry. There are reasons based on experiment for preferring the second alternative. Solutions of DNA in 0·2M-sodium chloride in water–glycerol (with up to 50% of glycerol) were examined by using DNA which had been treated with 5M-urea solution in the presence of 0·2M-sodium chloride, and untreated DNA. Fig. 2 shows the variation of $(\tan \alpha)_0$ [initial slope of plots of $\chi$ against velocity gradient ($G$) in the concentration-independent region of $\chi$] with solvent viscosity $\eta_0$. Comparison of the results with Cerf's predictions [5] and the results he quotes for tobacco-mosaic virus (a rigid

[3] Peterlin and Stuart, *Z. Physik*, 1939, **112**, 1, 129.
[4] Jordan, Mathieson, and Matty, *J.*, 1956, 158.
[5] Cerf, *Compt. rend.*, 1950, **230**, 81.

XUM

molecule) and polystyrene (a flexible molecule), also shown in Fig. 2, suggests that treatment with urea makes DNA molecules less rigid.

Calculations based on Peterlin's theory [6] for concentrated solutions, which is obeyed [7] by DNA, also suggest a decrease in molecular rigidity after treatment with urea. The value of $(\tan \Lambda)_0$ [the initial slope of the plot of $\chi$ against $(\eta - \eta_0)G/c$] for untreated DNA is $1{\cdot}66 \times 10^{-4}$ and for DNA treated with 5M-urea solution $(\tan \Lambda)_0 = 1{\cdot}16 \times 10^{-4}$. If the value of $(\tan \Lambda)_0$ is interpreted on a coiled model and a "stiffness factor," $\beta$, lying between 1 for a stiff coil and 3 for a soft coil, is defined as the ratio of the true molecular weight to that calculated on the assumption of complete rigidity,[7] then the decrease of $(\tan \Lambda)_0$ observed after treatment with urea requires an increase in $\beta$ and so a less rigid molecule.

Doty and Rice [8] maintained that treatment with urea has little or no effect on the molecular weight of DNA. Butler and Conway [1] suggested that urea causes a change in shape of DNA molecules by rupture of hydrogen bonds. Stacey and Alexander [9] reported that electron microscopy of herring-sperm DNA treated with urea revealed globular instead of fibrous particles, although their results on herring-sperm DNA imply that its behaviour towards urea is different from that of calf-thymus DNA.

The results of the measurements of streaming birefringence suggest that urea makes the DNA molecules more flexible and less asymmetrical. Some of the chain-linking hydrogen bonds may be broken by 5M-urea solution, leading to partial collapse of the molecule in spite of the overall charge reduction by sodium gegenions, from sodium chloride, which stabilises the intramolecular hydrogen bonds by reducing the repulsion of charged amino-groups. 1M-Urea solution cannot do this.

*Experimental.*—Viscosities were measured in a Couette-type apparatus.[10] Streaming birefringence was measured by adapting the viscometer as recommended by Ogston and Stanier.[11] The cylinders were of ebonite, the inner having a diameter of 1·097 cm. and the outer, 1·408 cm. The optical path length through the solution was 9·5 cm. and very low velocity gradients were used. Polaroids were used in place of Nicol prisms.

We thank the Department of Scientific and Industrial Research for a maintenance grant (to M. R. P.) and the British Empire Cancer Campaign (Nottinghamshire Branch) for generous financial assistance in the work of this and the following note. The experimental work of both notes was carried out in the Department of Chemistry, University of Nottingham.

UNIVERSITY COLLEGE, IBADAN, NIGERIA.
BRITISH NYLON SPINNERS LTD., PONTYPOOL, MON. [*Received, April 4th*, 1956.]

[6] Peterlin, *J. Polymer Sci.*, 1954, **12**, 45.
[7] Mathieson and Porter, *Biochim. Biophys. Acta*, 1954, **14**, 288.
[8] Doty and Rice, *ibid.*, 1955, **16**, 446.
[9] Stacey and Alexander, *Trans. Faraday Soc.*, 1957, **53**, 251.
[10] Mathieson and Matty, *J. Polymer Sci.*, 1957, **23**, 747.
[11] Ogston and Stanier, *Biochem. J.*, 1953, **53**, 4.

## 258. *Fractional Precipitation of Nucleic Acids by Ethanol.*

By A. R. Mathieson and M. R. Porter.

Fractional precipitation by hydrochloric acid of deoxyribonucleic acids (DNA) from various sources, followed by turbidity titration, has been described.[1] It has now been found possible to obtain stable suspensions by using ethanol as precipitant; the results are then different in some respects from those for precipitation with hydrochloric acid.

The following samples of nucleic acids were studied: three samples of DNA of high molecular weight ($\sim 6 \times 10^6$) prepared from calf-thymus by Gulland, Jordan, and Threlfall's method,[2] designated (i) S (supplied by Professor R. Signer) (ii) Al (prepared by Dr. S. Matty) and (iii) Gl(1) (prepared by the late R. H. Garner); (iv) a degraded sample of calf-thymus DNA obtained from B.D.H. Ltd. prepared by a method involving treatment with strong alkali; (v) herring-sperm DNA obtained from Glaxo Ltd.; (vi) DNA prepared from commercial wheat germ (" Froment ") by M. R. Porter by Daly, Allfrey, and Mirsky's method [3] and deproteinised by Sevag, Lackmann, and Smolens's method; [4] (vii) yeast rebonucleic acid (RNA) of low molecular weight prepared by Dr. A. S. Anderson.

Some results for the different samples of nucleic acids are illustrated, expressed as a percentage of the final turbidity. The curves fall into two sharply defined groups: (*a*) a set of very steep curves for the samples of high molecular weight and (*b*) much shallower curves for the others. In the presence of 0·2M-sodium chloride (as illustrated) less alcohol is required for precipitation than for aqueous solutions, *i.e.*, as for precipitations by hydrochloric acid.[1] The effect of previous thermal degradation (0·2M-sodium chloride solutions at 100° for times up to 1 hr.) of the samples of high molecular weight on precipitation by ethanol is complicated. When precipitation was carried out shortly after degradation the curves for the degraded materials were of the same shape as those for undegraded DNA and more alcohol was required, but the amount did not increase with increasing degradation. A mixture of degraded and undegraded DNA required even more alcohol. These results were unexpected but it was observed at the same time that addition of sodium chloride to a solution of thermally degraded DNA caused the viscosity to increase slowly, after its initial fall, becoming constant only after 48 hr. In view of this instability, which may be due to a slow dispersion of aggregates, precipitations by alcohol were carried out on degraded samples 48 hr. after degradation. Under these conditions the curves for thermally degraded DNA resembled those of group (*b*) in the Figure, the DNA being precipitated over a greater range of alcohol concentration than before degradation. More alcohol was required the greater the extent of degradation, and the curve for a mixture fell between the curves for undegraded and degraded DNA, being roughly the average of the two.

In precipitation by ethanol material of high molecular weight is precipitated first, and degraded material is precipitated over a wider range of alcohol concentration, the normal results for the precipitation of polymers, whereas hydrochloric acid first precipitates material of low molecular weight and degraded samples are precipitated over a narrower range of hydrochloric acid concentration. Salt facilitates precipitation in both cases. The mechanisms of the two precipitations are clearly different. With hydrochloric acid it is likely to be due to reduction of the overall charge of the nucleate ions by titration, and it seems that the overall molecular charge density must be greater the greater the size of the molecules. The greater range of ethanol concentration which will precipitate

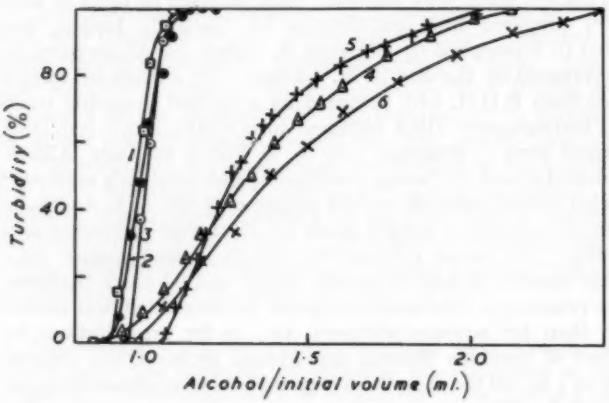
[1] Mathieson and Porter, *Nature*, 1954, **173**, 1190.
[2] Gulland, Jordan, and Threlfall, *J.*, 1947, 1129.
[3] Daly, Allfrey, and Mirsky, *J. Gen. Physiol.*, 1950, **33**, 497.
[4] Sevag, Lackmann, and Smolens, *J. Biol. Chem.*, 1938, **124**, 425.

XUM

degraded DNA suggests that degraded is more polymolecular than undegraded DNA. It is hoped to learn more about the mechanism by precipitating synthetic polyelectrolytes under these conditions.

*Experimental.*—A Spekker photoelectric absorptiometer with a blue filter was used for measuring the optical density of the solutions. Two kinds of cell were used, both permitting titration directly in the cell. The first, used for precipitation by hydrochloric acid, was

*Precipitation of different samples of nucleic acid by ethanol in 0·2M-sodium chloride. Concentration 0·072% in 0·2M-sodium chloride.*




(1) *Thymus nucleic acid; sample* Al.
(2) *Thymus nucleic acid; sample* S.
(3) *Thymus nucleic acid; sample* Gl(1).
(4) *Herring-sperm nucleic acid.*
(5) *Thymus nucleic acid. Sample B.D.H.*
(6) *Yeast ribonucleic acid.*

rectangular, of Perspex. The second, employed for precipitations with alcohol, was cylindrical and was thermostatted at 19°. In all cases precipitant was added dropwise from a microburette while the solution was stirred mechanically. It is most important to determine whether the turbid suspensions are stable (*i.e.*, have constant optical density) over a reasonable length of time. An individual experiment took 15—20 min., and reproducibility was attained when the optical density did not alter by more than 25% in 12 hr. Attempts to separate useful quantities of the turbid suspensions from these very dilute solutions (and they flocculate rapidly at higher concentrations) were not successful.

We thank Professor R. Signer for a sample of thymus DNA obtained through the courtesy of Professor D. O. Jordan, and Drs. S. Matty and A. S. Anderson for preparing some of the samples of nucleic acid.

University College, Ibadan, Nigeria.
British Nylon Spinners Ltd., Pontypool, Mon.

[*Received, April 4th*, 1956.]

## 259. *The Electrolytic Determination of Indium.*

By (the late) H. TERREY and J. THABIT.

THIEL [1] used silver electrodes in the quantitative electrodeposition of indium, because platinum was attacked. Kellock and Smith [2] recommended solutions containing Rochelle salt as giving the best results. Dennis and Geer [3] deposited indium from a solution containing pyridine, hydroxylamine, or formic acid; they also stated that no platinum black remained on the cathode after the metal was dissolved. We had determined indium by electrolysis in slightly acid solution, the platinum electrode being protected by prior deposition of copper.

*Experimental.*—It was found that in almost all cases the platinum cathode was attacked on dissolution of the deposited metal and we could not verify the statement [3] that the use of larger quantities of formic acid avoided the formation of platinum black.

It was found that all the suggested method required rather a long time (a few hours in some cases) to deposit 0·1 g. of indium, and there was no way of checking the end-point of electrodeposition.

To avoid attack of the platinum cathode and achieve conditions under which a few tenths of a gram of indium could be deposited quantitatively in a reasonable time, the following procedure was found satisfactory.

| In + Cu found (g.) | Cu added (g.) | In found (g.) | Mean value found | In calc. (g.) | In + Cu found (g.) | Cu added (g.) | In found (g.) | Mean value found | In calc. (g.) |
|---|---|---|---|---|---|---|---|---|---|
| 0·0396 | 0·0148 | 0·0248 | | | 0·1613 | 0·0372 | 0·1241 | | |
| 0·0394 | 0·0148 | 0·0246 | 0·0247 | 0·0248 | 0·1610 | 0·0372 | 0·1238 | 0·1239 | 0·1242 |
| 0·0396 | 0·0148 | 0·0248 | | | 0·1611 | 0·0372 | 0·1239 | | |
| 0·0767 | 0·0148 | 0·0619 | | | 0·2230 | 0·0372 | 0·1858 | | |
| 0·0767 | 0·0148 | 0·0619 | 0·0619 | 0·0621 | 0·2228 | 0·0372 | 0·1859 | 0·1858 | 0·1863 |
| 0·0766 | 0·0148 | 0·0618 | | | 0·2231 | 0·0372 | 0·1859 | | |

A known volume of standard copper sulphate (the copper content of which has been determined electrolytically) is added to indium sulphate solution. As little as 15 mg. of copper in 10 ml. of copper sulphate solution suffices to protect the platinum cathode. The solution is made basic with sodium hydroxide or ammonia, then just enough formic acid is added to make the solution acidic, discharge the blue colour, and redissolve the gelatinous precipitate.

By applying a potential of about 2 v, copper is deposited first; after all the copper has been deposited, the potential is increased to allow a current of 4—5 amp. to carry the indium on to the cathode.

Completion of deposition of indium can be detected by exposing a fresh area of the copper-plated cathode to the solution.

Finally the electrodes are washed repeatedly with distilled water, then with absolute alcohol without interruption of the current. Then the cathode is dried in an electric oven at 110—120°, allowed to cool, and weighed.

Dilute nitric acid is a good solvent for the deposit. If the potential is increased before all the copper has been deposited, a rather dark deposit is obtained, otherwise the deposit is silver-white.

Some typical results are tabulated.

COLLEGE OF ARTS AND SCIENCES,
BAGHDAD, IRAQ.
UNIVERSITY COLLEGE, LONDON.

[*Received, March 29th*, 1957.]

[1] Thiel, *Z. anorg. Chem.*, 1904, **39**, 119.
[2] Kellock and Smith, *J. Amer. Chem. Soc.*, 1910, **32**, 1248.
[3] Dennis and Geer, *ibid.*, 1904, **26**, 438.

XUM

## 260. *Hydroxyl Stretching Frequencies of Some Analogues of 8-Hydroxyquinoline.*

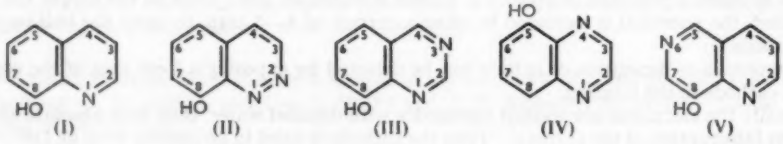
By F. J. C. Rossotti and Hazel S. Rossotti.

Rundle and Parasol [1] have found that the hydroxyl fundamental stretching frequency, $\nu$, of a number of hydrogen-bonded compounds decreases with decreasing length of the O–H–O bonds. A similar correlation between $\nu$ and the estimated O–H–O and O–H–N distances in several organic reagents for metal ions has been reported by Dyrssen.[2] The hydroxyl stretching frequency of 8-hydroxyquinoline and a number of its aza-analogues and related compounds have now been measured in carbon tetrachloride solution. The results are shown in the Table, together with values of the O–H force constant, $k$, calculated by using Hooke's relation for a simple harmonic oscillator.

| No. | Reagent, HA | $\nu$ (cm.$^{-1}$) (in $CCl_4$) | $10^{-5}k$ (dyne cm.$^{-1}$) | $pK_{OH}$ * (50% dioxan) | $pK_{NH}$ * |
|---|---|---|---|---|---|
| 1 | 8-Hydroxyquinoline (I) | 3419 | 6·59 | 10·80 | 4·48 |
| 2 | 8-Hydroxy-2-methylquinoline | 3415 | 6·57 | 11·01 | 5·01 |
| 3 | 8-Hydroxycinnoline (II) | 3433 | 6·64 | 8·84 | 1·77 |
| 4 | 8-Hydroxy-4-methylcinnoline | 3423 | 6·60 | 9·00 | 2·59 |
| 5 | 8-Hydroxyquinazoline (III) | 3454 | 6·57 | 9·59 | 3·30 |
| 6 | 8-Hydroxy-2 : 4-dimethylquinazoline | 3426 | 6·61 | 10·14 | 3·15 |
| 7 | 8-Hydroxy-4-methyl-2-phenylquinazoline | 3435 | 6·65 | 10·33 | <1 |
| 8 | 5-Hydroxyquinoxaline (IV) | 3465 | 6·77 | 9·29 | <1 |
| 9 | 8-Hydroxy-1 : 6-naphthyridine (V) | 3455 | 6·72 | 9·16 | 3·86 |

* Stoicheiometric values valid for 50% v/v aqueous dioxan containing 0·3M-sodium perchlorate at 20°. The values for reagent 9 are taken from ref. 4 and those for other reagents from ref. 3.

Although the dimensions of the heterocyclic skeleton are the same for all the reagents studied, the O–H stretching frequencies vary by as much as 50 cm.$^{-1}$, corresponding to a difference in force constant of $0{\cdot}2 \times 10^5$ dynes cm.$^{-1}$. The values of $\nu$, and hence of $k$, may be affected (i) by electromeric or inductive effects produced by the ring-nitrogen atoms or by methyl or phenyl substituents (cf. ref. 5), or (ii) by hydrogen-bonding through the hydroxyl group, or by a combination of these factors. If the former effects were




(I) (II) (III) (IV) (V)

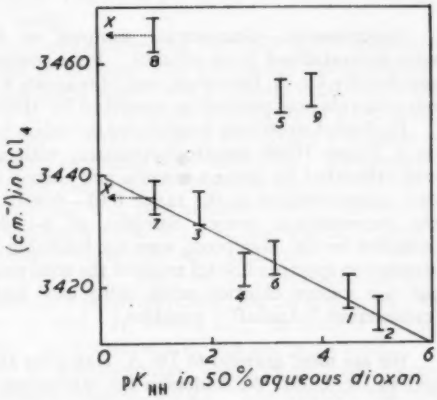
predominant, it might be expected that an increase in $\nu$ would be accompanied by an increase in the value of $pK_{OH}$ ($= \log [HA]/[H^+][A^-]$). However, no such correlation with $pK_{OH}$ is observed (see Table), and it may be assumed that the influence of electromeric and inductive effects on the hydroxyl stretching frequency is obscured by the formation of hydrogen bonds. Moreover, since the values of $\nu$ refer to dilute solution and are unaffected by changes in concentration, the differences presumably reflect the differing tendencies of the reagents to form intramolecular O–H–N bonds. Some measure of the affinity between nitrogen and hydrogen atoms in the various reagents is afforded

[1] Rundle and Parasol, *J. Chem. Phys.*, 1952, **20**, 1487.
[2] D. Dyrssen, *Rec. Trav. chim.*, 1956, **75**, 753.
[3] Irving and H. S. Rossotti, *J.*, 1954, 2910.
[4] H. S. Rossotti, D.Phil. Thesis, Oxford, 1954.
[5] Osborn, Schofield, and Short, *J.*, 1956, 4191.

XUM

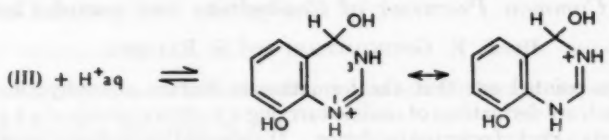
by the values of $pK_{NH}$ (= log $[H_2A^+]/[HA][H^+]$) in 50% aqueous dioxan, which are given in the Table. However, exact correlation of the O–H stretching frequency with $pK_{NH}$ could not be expected; not only do these quantities refer to different media, but the former value depends on the force between the hydroxylic-hydrogen atom and the adjacent nitrogen atom, while the latter describes the tendency of a solvated proton to react with the more basic of the two nitrogen atoms, regardless of its position in the ring.

The positions of the basic centres of the hydroxydiazines are uncertain. The suggestion [3] (based on the relative values of $pK_{NH}$ of 8-hydroxycinnoline and its 4-methyl derivative, and on the similarity between the ultraviolet absorption spectra of the




*Hydroxyl stretching frequencies in carbon tetrachloride of analogues of 8-hydroxyquinoline as a function of $pK_{NH}$ in 50% aqueous dioxan. The numbers of the reagents are those given in the Table.* (X = $pK_{NH} < 1$.)

8-hydroxycinnolinium and the 8-hydroxyquinolinium ion) that $N_{(1)}$ is the more basic centre in 8-hydroxycinnoline has recently been questioned.[6] It is probable [5] that the 8-hydroxyquinazolinium ion is hydrated in aqueous solution, and that the reaction of 8-hydroxyquinazoline with dilute acid involves addition of hydrogen to both $N_{(1)}$ and $N_{(3)}$. Methylation occurs at $N_{(3)}$ in 8-hydroxyquinazoline,[7] but at $N_{(1)}$ in some 4-substituted quinazol-




ines,[8] and spectrophotometric measurements [3] are compatible with the assignment of $N_{(1)}$ as the more basic centre in 8-hydroxy-2 : 4-dimethyl- and 8-hydroxy-4-methyl-2-phenyl-quinazoline. Results of both methylation [7] and spectrophotometric work [4] suggest that $N_{(6)}$ is the more basic nitrogen atom in 8-hydroxy-1 : 6-naphthyridine. Methylation occurs at $N_{(1)}$ in 5-hydroxyquinoxaline,[7] although the ultraviolet absorption spectra [3] of the 5-hydroxyquinoxalinium and the 8-hydroxyquinolinium ion are very similar.

The relation between hydroxyl stretching frequency and $pK_{NH}$ is shown in the Figure. The reagents fall into two groups, comprising (i) compounds 1, 2, 3, 4, 6, and 7 for which $\nu$ lies between 3415 and 3435 cm.$^{-1}$, and increases almost linearly with decreasing $pK_{NH}$ and (ii) compounds 5, 8, and 9, for which $\nu$ lies between 3454 and 3565 cm.$^{-1}$. Since the

[6] Osborn and Schofield, *J.*, 1956, 4207.
[7] Albert and Hampton, *J.*, 1954, 505.
[8] Morley and Simpson, *J.*, 1948, 360; 1949, 1354.

XUM

first group includes 8-hydroxyquinoline and its 2-methyl derivative, the observed correlation between $\nu$ and $pK_{NH}$ suggests that the latter value refers to the nitrogen atom adjacent to the hydroxyl group, *i.e.*, that $N_{(1)}$ is the more basic centre in 8-hydroxycinnoline, 8-hydroxy-4-methylcinnoline, and 8-hydroxy-2 : 4-dimethyl- and 8-hydroxy-4-methyl-2-phenyl-quinazoline. The values of $\nu$ for the second group of reagents lie about 30 cm.$^{-1}$ above the line through the first set of points indicating that weaker intramolecular O–H–N bonds occur in these compounds. These results are compatible with the observation [7] that methylation of 8-hydroxyquinazoline, 5-hydroxyquinoxaline, and 8-hydroxy-1 : 6-naphthyridine occurs at $N_{(3)}$, $N_{(1)}$, and $N_{(6)}$ respectively, and suggest that the nitrogen atoms adjacent to the hydroxyl groups are not the more basic centres in these reagents.

*Experimental.*—Commercial samples of 8-hydroxy- and 8-hydroxy-2-methyl-quinoline were recrystallised from ethanol. Pure specimens of reagents 3, 4, 5, 8, and 9 were kindly supplied by Dr. A. Hampton, and of reagents 6 and 7 by Dr. K. Schofield. Commercial carbon tetrachloride was purified as described by Hicks, Hooley, and Stephenson.[9]

Hydroxyl stretching frequencies in carbon tetrachloride solution were measured to $\pm 3$ cm.$^{-1}$ on a Hilger H800 spectrophotometer, with a lithium fluoride prism. The frequency scale was calibrated by using ammonia and carbon dioxide. Each reagent was studied for at least two concentrations in the range 0·01—0·001M, and the values of $\nu$ were reproducible within the experimental error. Samples of 8-hydroxy-1 : 5- and 8-hydroxy-1 : 7-naphthyridine (supplied by Dr. Hampton) were too insoluble in carbon tetrachloride to be investigated. The absorption spectra of Nujol mulls of the solid reagents were also measured in the range 1750—650 cm.$^{-1}$, a sodium chloride prism being used and a frequency scale calibrated against carefully fractionated " AnalaR " pyridine.

We are most grateful to Dr. A. Hampton and Dr. K. Schofield for gifts of hydroxydiazines, and to Dr. D. M. W. Anderson for calibrating the spectrophotometer.

Department of Chemistry, University of Edinburgh. [*Received, October 18th*, 1957.]

[9] Hicks, Hooley, and Stephenson, *J. Amer. Chem. Soc.*, 1944, **66**, 1064.

---

## 261. *A Common Precursor of Conhydrine and* pseudo*Conhydrine.*

By T. R. Govindachari and S. Rajappa.

Robinson [1] has pointed out that the formation in Nature of conhydrine and *pseudo*-conhydrine which are derivatives of coniine carrying a hydroxyl group at a β-position to the nitrogen, suggests a kind of oriented oxidation. It appeared likely that a laboratory analogy could be furnished by the rearrangement of 2-*n*-propylpyridine 1-oxide, since it has been reported by Berson and Cohen [2] that 4-picoline 1-oxide on rearrangement yields a mixture of 4-pyridylmethanol and 3-hydroxy-4-picoline. It has now been found that rearrangement of 2-*n*-propylpyridine 1-oxide yields a mixture containing 2-1′-hydroxypropylpyridine (49%) and 5-hydroxy-2-propylpyridine (2·5%). The structure of the former product was proved by reduction to (±)-conhydrine and comparison with an authentic sample.[3] The structure of the latter rests on positive colour reactions with ferric chloride and Folin–Denis reagent, the ultraviolet absorption spectrum exhibiting characteristic shifts in the maxima in neutral, acidic, and alkaline media expected for β-hydroxypyridines,[4] non-identity with 3-hydroxy-2-propylpyridine,[5] and agreement in

[1] Sir Robert Robinson, " The Structural Relations of Natural Products," Oxford, 1955, p. 64.
[2] Berson and Cohen, *J. Amer. Chem. Soc.*, 1955, **77**, 1281.
[3] Galinovsky and Mulley, *Monatsh.*, 1948, **79**, 426.
[4] Specker and Gawrosch, *Ber.*, 1942, **75**, 1338; Govindachari and Narasimhan, *J.*, 1953, 2635.
[5] Gruber, *Canad. J. Chem.*, 1953, **31**, 564.

XUM

melting point with 5-hydroxy-2-propylpyridine prepared by other methods.[6] Since the last compound has been reduced [6] to *pseudo*conhydrine, the present work constitutes yet another synthesis of the alkaloid.

*Experimental.*—*2-Propylpyridine 1-oxide.* 2-Propylpyridine [7] (5 g.) in acetic acid (25 ml.) containing 30% hydrogen peroxide (5 ml.) was heated at 70° for 3 hr. More hydrogen peroxide (3 ml.) was added and the mixture left at 70° for a further 12 hr. The solution was evaporated *in vacuo* with repeated additions of water to remove the last traces of acetic acid and hydrogen peroxide. The residual liquid in chloroform was treated with an aqueous paste of potassium carbonate. Filtration after 16 hr. and evaporation of the solvent, followed by vacuum-distillation of the residual oil, gave *2-propylpyridine 1-oxide* (4 g.), b. p. 102°/2 mm. (Found: C, 69·8; H, 7·8. $C_8H_{11}ON$ requires C, 70·1; H, 8·0%).

*Rearrangement of the N-oxide.* The oxide (3·9 g.) was refluxed for 1 hr. with acetic anhydride (20 ml.). The acetic anhydride was then distilled off *in vacuo*, and the residue transferred to a Vigreux flask and distilled at 2 mm., all the distillable liquid (3·9 g.) being collected. The total distillate was heated on a steam-bath for ½ hr. with potassium hydroxide (5 g.) in water (60 ml.) and alcohol (40 ml.) and left overnight at 30°. Next morning the alcohol was removed *in vacuo*, and the aqueous alkaline solution repeatedly extracted with chloroform. Evaporation of the dried ($Na_2SO_4$) extract and distillation gave the non-phenolic material (1·9 g.), b. p. 114°/15 mm. The residual aqueous alkaline solution was just acidified with concentrated hydrochloric acid, basified with ammonia, and thoroughly extracted with chloroform. Evaporation of the dried ($Na_2SO_4$) extract left the phenolic portion (150 mg.) as an oil.

(*a*) The phenolic portion: Sublimation at 150°/2 mm., followed by crystallisation from ether–light petroleum (b. p. 40—60°), gave 5-hydroxy-2-propylpyridine (100 mg.), m. p. 92—93° (Found: C, 70·2; H, 7·7. Calc. for $C_8H_{11}ON$: C, 70·1; H, 8·0%), $\lambda_{max.}$ (in EtOH), 285 mμ (log ε 3·41); (in EtOH–HCl), 295 mμ (log ε 3·60); (in EtOH–KOH), 310 mμ (log ε 3·42).

(*b*) The non-phenolic portion: This (1·9 g.) in N-hydrochloric acid (20 ml.) was hydrogenated at 55 lb. per sq. in., after addition of Adams catalyst (0·2 g.). The solution was then filtered, concentrated to a small volume (5 ml.), basified with sodium hydroxide solution, and repeatedly extracted with ether. The dried ($Na_2SO_4$) extract was distilled, the fraction boiling at 120°/20 mm. being collected. Recrystallisation from ether afforded (±)-conhydrine (0·8 g.), m. p. and mixed m. p. 99—100° (Found: C, 67·4; H, 11·6. Calc. for $C_8H_{17}ON$: C, 67·1; H, 11·9%).

We are grateful to Mr. S. Selvavinayakam for the analyses and to the Government of India for the award of a senior research scholarship (to S. R.).

PRESIDENCY COLLEGE, MADRAS, INDIA. [*Received, November 12th*, 1957.]

[6] Gruber and Schlögl, *Monatsh.*, 1949, **80**, 499; Marion and Cockburn, *J. Amer. Chem. Soc.*, 1949, **71**, 3402.
[7] Brown and Murphey, *ibid.*, 1951, **73**, 3308.

---

## 262. *Ring Expansion. Part III.*[1] *The Isomerisation of Dibenzylidene Derivatives of* cyclo*Hexanones.*

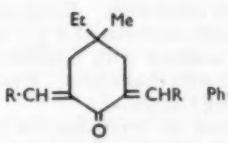
By R. H. BURNELL.

THE aromatisation of the dibenzylidene derivatives of *cyclo*hexanones was extended by Leonard and Robinson [2] to *cyclo*heptane-1 : 2-dione. Since this reaction appears to be related to the dienone–phenol isomerisation it was of interest to test its applicability to 4 : 4-disubstituted *cyclo*hexanone derivatives since aromatisation in such cases would

[1] Part II, *J.*, 1957, 3307.
[2] Leonard and Robinson, *J. Amer. Chem. Soc.*, 1952, **74**, 2143.

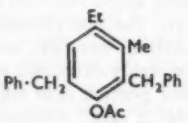
necessitate migration of one of the substituents. The benzylidene derivatives of 4-ethyl-4-methyl*cyclo*hexanone (Ia) and *spiro*[5 : 5]undecan-3-one (IIIa) were prepared and, on subjection to the reaction conditions employed by Leonard and Robinson,[2] gave products which from their infrared and ultraviolet spectra were aryl acetates. In the case of the *spiro*-compound (IIIa) there could be no ambiguity as to the structure of the product (IV), which was characterised by hydrolysis to the phenol and the preparation of a 3 : 5-dinitrobenzoate. The dibenzylidene derivative of 4-ethyl-4-methyl*cyclo*hexanone (Ia) on the other hand may have given a 3-ethyl-4-methylphenyl acetate rather than the isomer (II).

Arnold and Buckley[3] presented some evidence favouring a mechanism of pinacol–pinacone type for the dienone–phenol rearrangement but in the example cited (1 : 4-dihydro-4-methyl-1-oxo-4-phenylnaphthalene ⟶ 4-methyl-3-phenyl-1-naphthol) steric effects cannot be ignored. A simple case of the reaction was investigated, to compare the migratory aptitudes of methyl and ethyl groups in the dienone–phenol transformation. Dehydrobromination of the dibromo-ketone (V) afforded 4-ethyl-4-methyl*cyclo*hexa-

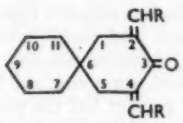



(Ia) : R = Ph

(Ib) : R = $CH_2O_2$:$C_6H_3$

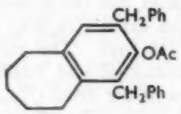



(II)

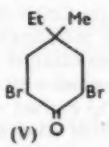



(IIIa) : R = Ph

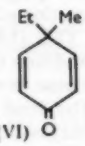
(IIIb) : R = $CH_2O_2$:$C_6H_3$



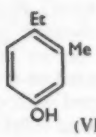

(IV)




(V)




(VI)




(VII)

2 : 5-dienone (VI) which was aromatised in acetic anhydride containing sulphuric acid. The hydrolysed product from the rearrangement was shown by analysis and spectral evidence to be a phenol isomeric with the ketone (VI). A sample of 3-ethyl-4-methylphenol was prepared from *m*-cresol acetate by low-temperature Fries rearrangement[4] and subsequent Clemmensen reduction:[5] comparison of it with the phenol obtained from the rearrangement of (VI) left no doubt as to their identity. The 3 : 5-dinitrobenzoates melted sharply at 130° alone or on admixture.

By analogy it can be assumed that the product obtained from the aromatisation of the ketone (Ia) is 2 : 6-dibenzyl-4-ethyl-3-methylphenyl acetate (II).

Dipiperonylidene*cyclo*hexanones were also prepared from *cyclo*hexanone, 4-ethyl-4-methyl*cyclo*hexanone and *spiro*[5 : 5]undecan-3-one. Under the conditions efficacious with the dibenzylidene derivatives, the first-mentioned dipiperonylidene derivative gave a low yield of an aryl acetate but in the other two cases only starting material was isolated, even when more vigorous conditions were employed.[6]

*Experimental.*—Ultraviolet spectra are for EtOH solutions unless otherwise stated.

*Diarylidenes.* The preparation is exemplified by the following: *spiro*[5 : 5]Undecan-3-one[7] (4·2 g.), piperonaldehyde (15 g.), and piperidine (5 c.c.) were refluxed for 6 hr. in absolute

[3] Arnold and Buckley, *J. Amer. Chem. Soc.*, 1949, **71**, 1781.
[4] Rosenmund and Schnurr, *Annalen*, 1928, **460**, 56.
[5] von Auwers and Mauss, *ibid.*, p. 240.
[6] Weiss and Ebert, *Monatsh.*, 1935, **65**, 399.
[7] Burnell and Taylor, *J.*, 1954, 3486.

ethanol (50 c.c.). Cooling and dilution with water gave yellow needles, m. p. 203° (from ethanol). Yields were usually high (*ca.* 80%) (see Table).

| Compound | M. p. | Calc. (%) C | H | O | Found (%) C | H | O | $\lambda_{max.}$ ‡ (ε) | ν(C=O) (cm.$^{-1}$) |
|---|---|---|---|---|---|---|---|---|---|
| (Ia) | 108° | 87·3 | 7·7 | 5·1 | 86·7 | 7·7 | 5·1 | 233 (14,010), 324 (23,700) | 1668 † |
| (IIIa) | 183 | 87·7 | 7·7 | 4·7 | 87·8 | 7·7 | 4·6 | 233 (15,700), 322 (22,300) | 1668 † |
| Dipiperonylidene derivatives: | | | | | | | | | |
| From *cyclo*hexanone | 189 | 72·9 | 5·0 | 22·1 | 72·7 | 5·0 | 22·0 | 261 (15,700), 371 (31,000) * | 1665 † |
| (Ib) | 184 | 74·2 | 6·0 | 19·8 | 74·0 | 6·0 | 19·9 | 261 (15,400), 370 (24,900) * | 1666 † |
| (IIIb) | 203 | 75·5 | 6·1 | 18·6 | 75·5 | 6·3 | 18·7 | 257 (15,500), 370 (24,800) * | 1664 † |

* Measured in $CHCl_3$. † KBr mull. ‡ In mμ.

*Aryl acetates.* The method was essentially that of Leonard and Robinson,[3] *e.g.*: the dibenzylidene derivative (Ia) (1·0 g.), acetic anhydride (3 c.c.), and acetic acid saturated with dry hydrogen bromide (5 c.c.) were mixed and kept at 65° for 15 hr. After cooling, the mixture was diluted with water and extracted with ether. The ethereal solution was washed free from acid, evaporated, and dried ($Na_2SO_4$), giving a dark yellow residue (0·91 g.) which was purified by evaporative distillation. The product, b. p. 248° (0·70 g.), had $\lambda_{max.}$ 307 mμ (ε 8000) and ν(C=O) 1760 cm.$^{-1}$ (and 1195 cm.$^{-1}$) (Found: C, 83·4; H, 7·5. $C_{25}H_{26}O_2$ requires C, 83·8; H, 7·3%).

1′ : 3′-*Dibenzyl*-2′-*hydroxybenzo*cyclo*heptene* (IV; R = H). The isomerisation product from the spiran (IIIa) was refluxed in 5% ethanolic potassium hydroxide (50 c.c.) for 4 hr. Dilution with water and ether-extraction furnished an oil, b. p. 285°, $\lambda_{max.}$ 288 mμ (ε 4610) and OH stretching band at 3470 cm.$^{-1}$ (no carbonyl absorption). Its 3 : 5-*dinitrobenzoate*, prepared in pyridine, had m. p. 158° (from ethanol) (Found: C, 71·6; H, 5·3. $C_{32}H_{26}O_6N_2$ requires C, 71·6; H, 5·3%).

2 : 6-*Dibromo*-4-*ethyl*-4-*methyl*cyclo*hexanone* (V). To a cooled solution of 4-ethyl-4-methyl-*cyclo*hexanone (2·8 g.) in acetic acid (15 c.c.) was added bromine (6·4 g.) in acetic acid (15 c.c.). Hydrobromic acid (3 c.c.) was added and the solution set aside for 4 hr. Dilution with water and ether-extraction gave a yellow oil (5·51 g.) which crystallised (m. p. 74°) from light petroleum (Found: C, 36·7; H, 4·6; Br, 53·5. $C_9H_{14}OBr_2$ requires C, 36·3; H, 4·7; Br, 53·7%).

4-*Ethyl*-4-*methyl*cyclo*hexa*-2 : 5-*dien*-1-*one* (VI). The dibromo-compound (VI) (3·0 g.) was refluxed in collidine (10 c.c.) for 4 min. The usual working up afforded a brown oil (1·25 g.) which was purified by chromatography over alumina. Elution with light petroleum (b. p. 60—80°) gave the dienone as a pale oil (1·01 g.), $\lambda_{max.}$ 234 mμ (ε 10,500), characterised as the unstable dark red 2 : 4-*dinitrophenylhydrazone*, m. p. 131° (from chloroform–ethanol), $\lambda_{max.}$ 256 and 390 mμ (ε 24,000 and 49,700 respectively) (Found: N, 17·8. $C_{15}H_{16}O_4N_4$ requires N, 17·7%).

3-*Ethyl*-4-*methylphenol* (VII). To the dienone (0·91 g.) in acetic anhydride (10 c.c.) was added sulphuric acid (3 drops) in acetic anhydride (3 c.c.). After 12 hr. water was added and the mixture kept in the cold overnight. Ether-extraction gave a yellow oil (0·77 g.) from which the phenol was obtained by alkaline hydrolysis; it had b. p. 226—228°, $\lambda_{max.}$ 286 mμ (ε 1600), and gave a 3 : 5-*dinitrobenzoate*, m. p. 130° (from ethanol) (Found: C, 57·9; H, 4·3; N, 8·4. $C_{16}H_{14}O_6N_2$ requires C, 58·2; H, 4·3; N, 8·5%). Admixture with an authentic sample (see text) of 3-ethyl-4-methylphenyl 3 : 5-dinitrobenzoate (m. p. 130°) caused no depression in the m. p. and the infrared spectra of the phenols were identical.

The author is indebted to Mr. D. Taylor for technical assistance and to Mr. A. W. Sangster for the infrared spectra.

Department of Chemistry, University College of the West Indies,
Mona, St. Andrew, Jamaica, B.W.I. [*Received, November 15th*, 1957.]

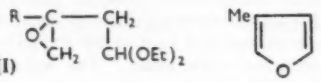
XUM

## 263. *A Short Synthesis of 3-Methylfuran.*

By J. W. Cornforth.

Several 3-monosubstituted furans have been recognized among natural products, but only two 3-monoalkylfurans, 3-methyl-[1] and 3-*iso*propyl-furan,[2] have been synthesized; and these always by removal of other substituents from an existing furan ring. The overall yields are uniformly bad.

3 : 4-Epoxy-3-methylbutanal diethyl acetal (I; R = Me) is now readily available[3] from the reaction of 2-methylallyl chloride with magnesium and ethyl orthoformate, followed by oxidation of the product by perphthalic acid. Boiling this epoxy-acetal with




0·1N-sulphuric acid gave 3-methylfuran (II) in 57% yield. Acetic acid (0·5N) seemed to be somewhat less effective than the mineral acid. More than one mode of cyclization could be postulated, and more than one may actually operate.

2-Methylallyl chloride is exceptional among 2-substituted allyl halides in being available commercially; a useful general synthesis of 3-monosubstituted furans based on this cyclization must await general methods for preparing substances of type (I).

*Experimental.*—3 : 4-Epoxy-3-methylbutanal diethyl acetal (10 g.) and 0·1N-sulphuric acid (1 l.) were heated under a fractionating column for 3 hr., the *methylfuran* and ethanol being removed intermittently by distillation. The distillate was washed once with half-saturated aqueous calcium chloride (20 ml.) and twice with a little saturated aqueous ammonium chloride, dried by boiling with sodium, and redistilled, to give 3-*methylfuran* (2·7 g.), b. p. 65—65·5°/749 mm., $n_D^{19}$ 1·4330 (Found: C, 73·2; H, 7·4. $C_5H_6O$ requires C, 73·1; H, 7·3%). (This appears to be the first published analysis of synthetic 3-methylfuran.) The refractive index is higher than that given by Asahina [4] ($n_D^{18}$ 1·4255). The pine-splinter test and the colours with vanillin in hydrochloric acid were as recorded.[4] With an Ehrlich's reagent made from *p*-dimethylaminobenzaldehyde (0·2 g.), acetic acid (9·5 ml.), and hydrochloric acid (0·5 ml.),[5] 3-methylfuran in acetic acid gave a pink colour slowly changing (more rapidly with excess of reagent or more hydrochloric acid) to intense green. Furan treated similarly gave, more slowly, an orange-pink colour changing to green.

I thank Mrs. B. Jarrett for the analysis.

National Institute for Medical Research,
London, N.W.7.

[*Received, December 3rd,* 1957.]

[1] Reichstein and Zschokke, *Helv. Chim. Acta*, 1931, **14**, 1270; Rinkes, *Rec. Trav. chim.*, 1931, **50**, 1127; Gilman and Burtner, *J. Amer. Chem. Soc.*, 1933, **55**, 2903.
[2] Gilman, Calloway, and Burtner, *ibid.*, 1935, **57**, 906.
[3] Cornforth and Firth, *J.*, 1091.
[4] Asahina, *Acta Phytochim.*, 1924, **2**, 1; *Chem. Zentr.*, 1924, II, 1694.
[5] Morgan and Elson, *Biochem. J.*, 1934, **28**, 988.

## 264. *Preparation of Ketones by Cleavage of 2 : 4-Dinitrophenylhydrazones.*

By N. M. Cullinane and B. F. R. Edwards.

2 : 4-Dinitrophenylhydrazones are frequently used for the characterization of ketones. In particular *o*-hydroxy-ketones, prepared, for example, by the Fries reaction, tend to be oils and can be determined quantitatively in this way.[1] Regeneration of the initial ketones is thus a matter of considerable interest, and a number of such preparations, including those of *o*- and *p*-hydroxy-ketones, have now been carried out, with very good yields.

Recent methods for the recovery of ketones include treatment of the dinitrophenylhydrazones with formic acid and copper carbonate,[2] and with acid stannous chloride.[3]

*Experimental.—2-Hydroxy-3-methylacetophenone.* The 2 : 4-dinitrophenylhydrazone [4] (4 g.) was boiled with acetone (500 c.c.) under reflux until a clear solution resulted. Stannous chloride dihydrate in concentrated hydrochloric acid (80 c.c.) and water (120 c.c.) was introduced at once and refluxing continued (for time see Table). The solution was then cooled and made alkaline with 2N-sodium hydroxide. The acetone was removed on a water-bath; excess of concentrated hydrochloric acid was added to the cooled product, which was then distilled with steam. The ketone was extracted from the steam-distillate with benzene and purified in the usual way; it had b. p. 107°/12 mm.[5] The quantity of stannous chloride and the duration of the reaction are seen from the Table to have a considerable influence on the yields.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Time (min.) ..... | 65 | 45 | 30 | 20 | 30 | 30 | 30 | 30 | 30 |
| $SnCl_2,2H_2O$ ..... | 10 | 10 | 10 | 10 | 4 | 5 | 6 | 6·5 | 7 |
| Yield (%) ..... | 8·5 | 25 | 55 | 23 | 15 | 45 | 70 | 81 | 70 |

*Benzophenone.* The dinitrophenylhydrazone was not very soluble in acetone and the yields obtained in this solvent were not very good. Substituting acetic acid improved the yields. The hydrazone (4 g.) in hot glacial acetic acid (400 c.c.) was treated with stannous chloride (13 g.) in concentrated hydrochloric acid (80 c.c.) and water (120 c.c.) and boiled for 1 hr. Excess of 2N-sodium hydroxide was added to the cooled product, and the ketone driven over with steam and purified (yield, 88%). When stannous chloride (*a*) (20 g.) and (*b*) (13 g.) was used and the refluxing continued for 30 min. the yields were 19% and 23% respectively.

*Acetophenone.* The dinitrophenylhydrazone, m. p. 236°, was treated as was the derivative of benzophenone except that heating was for only 30 min. Distillation with steam, etc., gave a 95% yield of ketone.

o-*Hydroxybenzophenone.* The m. p. of the 2 : 4-dinitrophenylhydrazone is given as 250—251° by Johnson; [6] we obtained brick-red plates (from ethyl acetate), m. p. 260° (Found: C, 59·6; H, 3·9; N, 14·7. Calc. for $C_{19}H_{14}O_5N_4$: C, 60·3; H, 3·7; N, 14·8%); the compound was heated as just described, for 1 hr.; excess of sodium hydrogen carbonate was added to the cooled product which was then distilled with steam, giving a 73·5% yield of *o*-hydroxybenzophenone,[7] m. p. 39°.

*2-Hydroxy-5-methylacetophenone.* The dinitrophenylhydrazone [6, 8] was boiled under reflux for 30 min. with the same quantities of reactants as above (when the acetic acid was replaced by acetone the yield of ketone was considerably reduced). Addition of sodium hydrogen carbonate and distillation with steam gave an 80% yield of the hydroxy-ketone,[9] m. p. 50°.

p-*Hydroxybenzophenone.* The dinitrophenylhydrazone, brick-red needles (from aqueous alcohol [10]), m. p. 240° (Found: C, 60·1; H, 3·7; N, 14·4. Calc. for $C_{19}H_{14}O_5N_4$: C, 60·3; H,

[1] Cullinane, Evans, and Lloyd, *J.*, 1956, 2222.
[2] Robinson, *Nature*, 1954, **173**, 541.
[3] Demaecker and Martin, *Nature*, 1954, **173**, 266.
[4] Cullinane, Lloyd, and Tudball, *J.*, 1954, 3894.
[5] Anschütz and Scholl, *Annalen*, 1911, **379**, 342.
[6] Johnson, *J. Amer. Chem. Soc.*, 1951, **73**, 5888.
[7] Winkler, *Arch. Pharm.*, 1928, 48.
[8] Cullinane and Edwards, *J.*, 1957, 3018.
[9] von Auwers and Müller, *Annalen*, 1909, **364**, 147.
[10] Pallares and Garza, *Arch. Inst. Cardiol. Mexico*, 1947, **17**, 833.

XUM

3·7; N, 14·8%), was treated in the same way as the *o*-hydroxy-derivative, except that the product, after addition of sodium hydrogen carbonate, was extracted with benzene, and the solution shaken with 2N-sodium hydroxide. Distillation with steam removed traces of benzene, and acidification of the alkaline solution with concentrated hydrochloric acid precipitated the ketone as colourless needles (93·5%), m. p. 135°.[11]

p-*Hydroxyacetophenone*. The 2 : 4-dinitrophenylhydrazone,[12] deep red prisms (from alcohol), m. p. 269° (Found: C, 53·4; H, 3·8; N, 18·0. Calc. for $C_{14}H_{12}O_5N_4$: C, 53·1; H, 3·8; N, 17·7%), treated as described for the benzophenone derivative, gave a product from which the acetic acid was removed in steam; the residue was extracted with benzene, and the extract shaken with 2N-sodium hydroxide. Acidification of the alkaline solution with concentrated hydrochloric acid gave colourless needles (65·9%), m. p. 108°.[13]

p-*Hydroxybutyrophenone*. In the same way the 2 : 4-dinitrophenylhydrazone,[12] red prisms (from alcohol), m. p. 223° (Found: C, 56·0; H, 4·9; N, 16·2. Calc. for $C_{16}H_{16}O_5N_4$: C, 56·0; H, 4·7; N, 16·3%), gave the hydroxy-ketone,[14] colourless needles (96·8%), m. p. 91°.

Yields in the above experiments were accurately determined by reconversion of the ketones into their 2 : 4-dinitrophenylhydrazones.

One of us (B. F. R. E.) thanks the University of Wales for a Post-Graduate Studentship.

UNIVERSITY COLLEGE, CATHAYS PARK, CARDIFF. [*Received, December 2nd*, 1957.]

[11] Fischer, *Ber.*, 1909, **42**, 1017.
[12] Dutton, Briggs, Brawn, and Powell, *Canad. J. Chem.*, 1953, **31**, 837.
[13] Mozingo, *Org. Synth.*, 1941, **2**, 45.
[14] Perkin, *J.*, 1889, **55**, 546.

---

## 265. 8-*Amino*isoquinoline: *A Correction.*

By K. SCHOFIELD.

RECENTLY [1] the basic strengths of *iso*quinoline ($pK_a$ 5·40) and 8-amino*iso*quinoline ($pK_a$ 6·06) were correctly reported, but $\Delta pK_a$ for the pair was given as 1·66 (Ref. 1, Table 2) instead of 0·66. 8-Amino*iso*quinoline would be expected to be appreciably stronger than its parent base because of the possibility of resonance in its cation involving *o*-quinonoid forms. In fact $\Delta pK_a$ for 8-amino*iso*quinoline is smaller than $\Delta pK_a$ (0·80) [1] for 7-amino*iso*quinoline, an isomer from which the additional possibilities for resonance are absent. The pair of isomers, 8- and 7-amino*iso*quinoline ($\Delta pK_a$ 0·66 and 0·80) is thus analogous to the pair, 5- and 6-aminoquinoline ($\Delta pK_a$ 0·52 and 0·69), and both cast doubt on the significance of *o*-quinonoid resonance forms. It is significant that the infrared N–H force constants are lower than expected [1] in both 8-amino*iso*quinoline and 5-aminoquinoline.

WASHINGTON SINGER LABORATORIES,
PRINCE OF WALES ROAD, EXETER. [*Received, December 2nd*, 1957.]

[1] Osborn, Schofield, and Short, *J.*, 1956, 4191.

XUM

XUM

XUM

# THE CHEMICAL SOCIETY

*PATRON*

HER MAJESTY THE QUEEN

*President*

E. L. Hirst, C.B.E., D.Sc., LL.D., F.R.S.

*Vice-Presidents*

*who have filled the office of President*

Sir Ian Heilbron, D.S.O., D.Sc., LL.D., F.R.S.
Sir Cyril Hinshelwood, M.A., Sc.D., F.R.S.
Sir Christopher Ingold, D.Sc., F.R.I.C., F.R.S.
W. H. Mills, M.A., Sc.D., F.R.S.
Sir Eric Rideal, M.B.E., M.A., D.Sc., F.R.S.
W. Wardlaw, C.B.E., D.Sc., F.R.I.C.

*Vice-Presidents*

Wilson Baker, M.A., D.Sc., F.R.S.
R. D. Haworth, D.Sc., Ph.D., F.R.S.
E. D. Hughes, D.Sc., F.R.I.C., F.R.S.
M. Stacey, Ph.D., D.Sc., F.R.S.
L. E. Sutton, M.A., D.Phil., F.R.S.
Sir Alexander Todd, M.A., D.Sc., F.R.S.

*Honorary Treasurer*

M. W. Perrin, C.B.E., M.A., F.R.I.C.

*Honorary Secretaries*

F. Bergel, D.Phil.Nat., D.Sc., F.R.I.C.
J. Chatt, M.A., Sc.D., F.R.I.C.
M. J. S. Dewar, M.A., D.Phil.

*Ordinary Members of Council*

D. W. Adamson, M.Sc., D.Phil., A.R.I.C.
R. G. R. Bacon, Ph.D., A.R.C.S.
G. R. Barker, B.Sc., Ph.D.
R. M. Barrer, D.Sc., Sc.D., F.R.S.
F. Bell, D.Sc., F.R.I.C., F.R.S.E.
A. J. Birch, M.Sc., D.Phil.
V. M. Clark, M.A., Ph.D.
A. G. Evans, Ph.D., D.Sc., F.R.I.C.
A. Hickling, D.Sc., Ph.D., F.R.I.C.
L. Hunter, Ph.D., D.Sc., F.R.I.C.
A. W. Johnson, Sc.D., Ph.D., A.R.C.S.
J. D. Loudon, Ph.D., D.Sc.
B. Lythgoe, M.A., Ph.D., F.R.I.C.
A. Maccoll, M.Sc., Ph.D.
R. S. Nyholm, M.Sc., D.Sc., F.R.I.C.
F. H. Pollard, B.Sc., Ph.D.
R. E. Richards, M.A., D.Phil.
L. A. K. Staveley, M.A.
J. C. Tatlow, Ph.D., D.Sc., F.R.I.C.
W. Wild, B.Sc., Ph.D., A.R.I.C.
G. T. Young, Ph.D., M.A., F.R.I.C.

*General Secretary*

J. R. Ruck Keene, M.B.E., T.D., M.A.

*Librarian*

R. G. Griffin, F.L.A.

*Deputy Librarian*

J. Bird

XUM

THE CHEMICAL SOCIETY

*'SPECIAL PUBLICATION' NO. 5*

**ANTIBIOTICS AND MOULD METABOLITES**

This report of a Symposium held in Nottingham on 26th March, 1956, is the fifth in The Chemical Society's series of Special Publications. The following are the main contributions:—

" Fungal quinones," by J. H. Birkinshaw (London).

" Synthesis of some fungal metabolites," by D. H. R. Barton (Glasgow).

" Azaphilones, a general survey," by A. D. G. Powell, A. Robertson, and W. B. Whalley (Liverpool).

" The structure of purpurogenone," by J. C. Roberts (Nottingham).

" Progress in the chemistry of oxytetracycline and related compounds," by L. H. Conover (Chas. Pfizer & Co. Ltd., Connecticut).

" Actinomycin," by A. W. Johnson (Nottingham).

" Chemistry of the cephalosporins," by E. P. Abraham and G. G. F. Newton (Oxford).

*Price: 15s.*

THE CHEMICAL SOCIETY
BURLINGTON HOUSE, LONDON W.1.

*Printed in Great Britain by Richard Clay and Company, Ltd., Bungay, Suffolk.*

XUM

XUM